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NUTRITION PRACTICE POINTS

By Dr. Nandita Palshetkar

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Importance and benefits of protein, vitamins and minerals (PVMs) in PREGNANCY AND LACTATION

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Dear FOGSIANs,

It gives me great pleasure to launch this last TOG NPP document. Significance of nutrition has been one of the priorities of the WE FOR STREE campaign. Knowing the correct nutritional requirements in pregnancy and lactation will now become easier.

These practice points will definitely help in further strengthening the WE FOR STREE campaign.

Happy reading and implementing !.

Best wishes!

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Importance and benefits of protein, vitamins, and minerals (PVMs) in pregnancy and lactation

1. Introduction

Pregnancy is a period in which physiological changes are rapid from the time of conception to birth. During pregnancy, nutritional requirements increase to promote maternal metabolism and tissue growth while supporting fetal growth and development.[1] Fetal growth is largely regulated by maternal nutrition and mediated by the maternal and fetal glucose/insulin/ insulin-like growth factor (IGF) axis.[2] The in utero environment influences fetal development and has a lasting influence on offspring and their future disease risk.[3] During pregnancy and lactation, there is an increased need of energy, proteins, various vitamins, and minerals as mother's nutrition is the only way to supplement nutritional requirements of the fetus. Moreover, after delivery the newborn will be dependent on the mother for his or her nutritional requirements that supports its growth and development. In few studies it was found that nutritional intake by the mother especially protein intake shows a strong association of childs weight and length up to 5 years of age. Hence, early life nutrition in a child's life is very crucial and should be first priority in the healthcare management of pregnancy and lactation.[1]

"A poor dietary intake of macronutrients (Protein) and micronutrients (Vitamins and Minerals) deficiency can have a significant impact on pregnancy and neonatal health outcomes."

2. Need for the document

There is an increased energy requirement in healthy pregnancies as basal metabolic rate and protein deposition is increased. Inadequate energy or protein intakes in pregnancy have been linked with an increased risk of non-communicable diseases such as type 2 diabetes and obesity in the offspring.[1] Moreover, changing food and lifestyle habits in both rural and urban areas of India are low on protein intake, hence proper diet and nutrition; especially in women during pregnancy is recommended.[4] During pregnancy there is a higher requirement for protein, vitamins and minerals (PVMs). The requirements for PVMs is further increased in the lactation period in comparison to those required in pregnancy, except few vitamins such as A, D, and K, calcium, fluoride, magnesium, and phosphorus.[5] Therefore, there is a need for healthy dietary guidelines along with a strong emphasis on regular physical exercise.[4]

"In terms of nutrition, pregnancy and lactation is a state of increased demand for energy, proteins, vitamins, and minerals to support the growing fetus and thereafter the demands of lactation."

Deficiency of macronutrients, micronutrients and its complications in pregnancy and lactation

Suboptimal micronutrient status may affect the risk of adverse pregnancy outcomes. This is because many of the physiological pathways can be disrupted by even the smallest disturbance in the micronutrient homeostasis. There is growing evidence that maternal nutritional status can alter the epigenetic state of the fetal genome. Thus, governing bodies recommend that pregnant women increase their daily intake of most micronutrients.

Insufficient calories, macro- and micronutrients can lead to deficiencies in building materials for the development and growth of the fetus.

- Iron deficiency in pregnancy increases perinatal morbidity and mortality. It is associated with higher risk of anemia in the mother, preterm birth, and low birth weight (LBW) of the newborn.[6]
- Daily iron supplementation reduced the risk of maternal anemia at term by 70% and iron deficiency at term by 57%.[7]
- Maternal vitamin D deficiency in pregnancy has been associated with the onset of diseases later in life, including autoimmune diseases, asthma, and type 1 diabetes.[6]
- Hypocalciurea can cause pre-eclampsia, and measuring urinary calcium/creatinine ratio in early pregnancy is a possible predictor of pre-eclampsia.[6]
- Maternal iodine deficiency may cause irreversible damage to a child's normal physical growth and mental development as iodine is necessary for brain development in utero.[6]
- Zinc deficiency is associated with adverse pregnancy outcome and poor fetal development.[6]
- Selenium deficiency in pregnancy has been associated with miscarriage, pre-eclampsia, and fetal growth restriction.[6]

Consequences of maternal malnutrition

Consequences for maternal health
- Anemia
- Increased infection
- Lethargy and weakness, lower productivity
- Increased risk of maternal complications and mortality

Consequences for fetal health
- Birth defects
- Cretinism
- IUGR, LBW, and prematurity
- Increased risk of infection
- Increased morbidity and mortality of fetus, neonates, and infants

- Deficiency of vitamin B 12 causes macrocytic anemia, neurologic dysfunction, and biochemical abnormalities associated with a higher risk of multiple adverse outcomes of pregnancy like intrauterine growth retardation (IUGR), LBW, pregnancy-induced hypertension, neural tube defects, and preterm delivery.[8]

Pregnant women may be at risk of nutritional deficiency hence, adequate nutrition should be provided to support the demand.

3. Pregnancy and protein metabolism

Adaptation of maternal metabolism occurs during pregnancy to ensure that fetus is continuously supplied with nutrients to sustain its exponential growth. The protein turnover is vital for the development of the fetus and should be sustained through active amino acid transfer from the maternal circulation. Metabolic changes that improve both dietary protein utilization and nitrogen retention must fulfil the enhanced demands of late pregnancy to satisfy fetal demands. In late pregnancy, the increased nitrogen retention is estimated to be due to a reduction in urinary nitrogen excretion as a result of decreased urea synthesis. Pregnancy is correlated with hypoaminoacidemia, even though the changes in protein metabolism during the late pregnancy favor the conservation of nitrogen. [9]

An increased turnover of proteins is seen in early pregnancy as compared to non-pregnant women. Also, increase in protein synthesis was reported by 15% in the second and 25% during the third trimester.

Metabolic adaptation in protein metabolism indicates that general physiological changes act to conserve protein and nitrogen during pregnancy, promote protein accretion, and ensure an adequate supply of nutrients to the fetus. [10]

- If the nutritional consumption of protein is below the certain threshold needed for metabolic adaptation, then women are at enhanced risk of poor pregnancy outcomes.[10]

- It is essential to identify the optimal protein and amino acid requirements during different stages of pregnancy to create adequate dietary intake recommendations.[10]

Benefits of balanced protein energy supplementation in pregnant women and fetal physical growth:

- A balanced protein energy supplementation during pregnancy improves fetal growth and increases infants' birth weight. Some studies have shown that supplements of more than 700 kcal/day[11] and containing up to 25% of energy as protein,[12] provided to women during pregnancy reduce the risk of LBW in the baby by 32% in certain contexts.[11]
- Content of protein in the supplement has also been shown to influence fetal growth.[13]
- Balanced protein energy supplementation during pregnancy containing 12.3% of protein produced higher fetal growth compared to supplementation containing 22.4% of protein.[13]

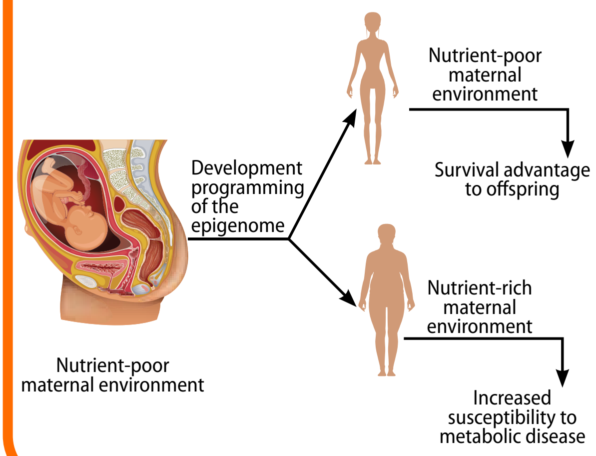
> *Improving maternal nutritional balance could be beneficial in improving pregnancy outcomes and fetal growth.*

Epigenetic changes during pregnancy

Poor nutritional status during development can result in structural and functional alterations that can persist throughout life in the key organs such as the liver, brain, muscle, pancreas, and adipose tissue. This subject is currently often referred to as the "predictive adaptive response" (PAR) hypothesis that denotes the processes by which the developing organism draws from early-life experience to exhibit a phenotype increasing the fitness based on expected future environmental conditions. In particular, poor or unbalanced nutrient intake during intrauterine development can impair fetal growth resulting in IUGR and also cause fetal adipose tissue and pancreatic beta-cell dysfunction (Figure 1).[14]

Plasticity of the epigenome during development may result in developing organism to "preadapt" to the future adult environment providing a

Figure 1 The thrifty phenotype hypothesis – Epigenetic changes (nutrient deficiency prone to metabolic diseases)



survival advantage. However, in cases where the fetal environment does not match the adult environment—or else, fetal development in a nutrient-poor environment (such as maternal starvation) coupled with a nutrient-rich adult environment—the resulting "catch-up" growth and disconnection among fetal programming and the adult environment can predispose to adult metabolic diseases such as obesity and type II diabetes. Hence, a causal link between epigenetic disturbances during development and the risk for metabolic disorders exists that may be initiated due to exposure to the nutrient-poor maternal environment.[14]

4. Nutritional requirements in pregnancy

Protein is an essential component of the human diet that supports growth and maintenance. Adequate dietary protein is essential during pregnancy to ensure a healthy outcome. The deposition of proteins in maternal and fetal tissue differs, with non-significant deposition in the first trimester, increases gradually during the second, and majority in the third trimester. Thus, protein intake recommendations should be gestational stage-specific with adequate energy to ensure that all requirements are met.[10]

According to the dietary guidelines for Indians by National Institute of Nutrition (NIN) and Indian Council of Medical Research (ICMR), the daily diet of a woman without any complications and healthy weight (ideal

BMI) should contain 0.5 g of protein during the first trimester and 6.9 g during the second trimester and 22.7 g during the third trimester of pregnancy.[4]

Micronutrients are essential vitamins and minerals that the human body requires to ensure normal metabolism, physical growth, and development. Inadequate intake of certain foods and poor quality of the diet can lead to micronutrient deficiency. Hence, supplementation with multiple-micronutrient is beneficial to overcome the deficiency.[15] Vitamins A, D, E, folate, B12, B6, and calcium, iron, zinc, iodine, copper, and selenium are the most commonly provided micronutrients during pregnancy as supplements.[1]

The need for most of the nutrients is increased during pregnancy to meet the high demands of both the growing fetus and the mother. An estimated fetal protein requirement is about 440 g throughout pregnancy and the placental protein requirement to be an additional 100 g. According to the assumptions, a 15% variation in birth weight exists and dietary protein is converted at 70% efficiency. Hence, the requirement for protein would be an additional 6.0 g/day averaged over pregnancy, but the demand is highest (10.7 g/day) in the last trimester.[16,17]

- Similarly, supplementing 20 g of protein and 150 kcal of energy per day showed an about 50 g increase in birth weight but did not affect the gestational duration. International guidelines recommend increased protein intake during pregnancy, especially during the second and third trimesters to ensure the additional 21 g needed for maternal and fetal tissues and placenta.[18]

> ***"If the mother has less nutrient intake during lactation, breast milk would draw from maternal body stores. Therefore, nutritional supplementation is beneficial."***

5. Physiology of milk production

Milk production and secretion is a complex physiological process resulting from both the previous development of the mammary gland and tight regulations by systemic hormones and local factors. All these aspects contribute to the coordinated secretory functioning of the mammary epithelial cells to provide milk of adequate composition and in sufficient quantity to the new-born. Colostrum is produced during the first 4 days postpartum, followed by a 10 to 15 days period of transitional milk secretion, before copious production of mature milk (after 15 days). Milk composition is dramatically altered: sodium and chloride concentrations fall while those of lactose, immunoglobulin A (IgA), lactoferrin (LTF), and other components of mature milk increase.[19]

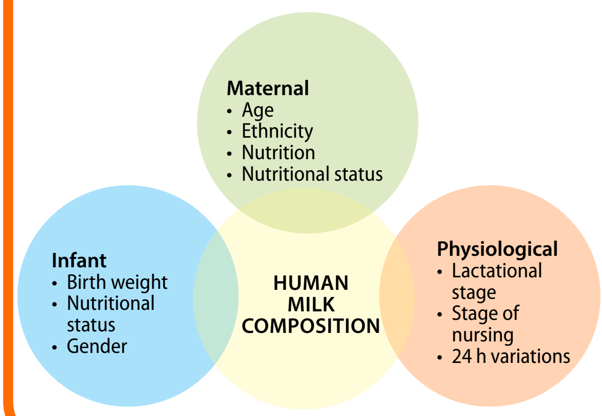
The nutrient composition of human milk is strongly influenced by the stage of lactation. These changes are consistent with consuming decreasing quantities of milk and ingesting other foods throughout lactation as the infant matures. The composition of milk at the time of weaning from extended nursing is different in comparison to that of exclusive breastfeeding. Whereas the concentration of lactose decreases fivefold during mammary involution, the concentration of proteins increases six-fold during this period. There is a high content of antibacterial proteins during mammary involution, which provides the breast with protection against infection at a time when milk stasis favors bacterial growth, and would also favor those ill toddlers who return to the breast during weaning.[20]

The nutrient composition of milk varies dramatically influenced by the length of lactation. Milk also improves the survival of the offspring by stimulating immunological competence. On average, the milk protein concentration during the later stages of lactation is sensitive to the declining output of milk.[20]

The impact of maternal nutrition on the composition of breast milk

Human milk is the best nutrition source for infants, as it contains the right balance of essential nutrients and other bioactive factors such as hormones, antibodies, bioactive molecules, and stem cells. Human milk composition changes dynamically as it is produced by women with significantly varying genotypes and phenotypes compared to infant formulas having standardized compositions. Human milk composition influenced by the maternal, infant, and physiological factors are depicted in Figure 2.[21]

Figure 2 Maternal, infant, and physiological factors that may influence human milk composition[21]



> ***Exclusive breastfeeding is recommended for the first 6 months of life and is associated with decreased incidence of infections and chronic diseases.***

A maternal diet can influence maternal milk composition through various interlinked metabolic pathways. These pathways modulate certain human-milk components directly via dietary intake leading to increment of the fatty acids levels and some other fat- and water-soluble vitamins (vitamins A, C, B-6, and B-12). In contrast, human milk's mineral content is generally considered less related to maternal dietary intakes.[22]

Current dietary intake, nutrient stores, and alterations in nutrient utilization are the three aspects of maternal nutrition that could have an impact on human milk composition. This alteration may have positive, neutral, or negative consequences to the infants. In case the mother's nutrition is continuously affected, but the nutrient concentrations in milk and milk volumes remain unchanged, then maternal stores or tissues will be depleted. Therefore, lactating mothers should be supplemented with required nutrient supplementation to fulfill their own needs and needs of the feeding baby through healthy breast milk.[23]

Fourth trimester is critical transition period with unmet maternal health requirements

Apart from the three trimesters of pregnancy and lactation period, very little is known about a critical and equally important period in women's lives that may require special care and attention. Most women and even some medical professionals do know very little about the fourth trimester.[24] The fourth trimester denotes the transition period after childbirth when infants are adjusting to life outside the womb and mothers to parenthood. The fourth trimester is marked by significant biological, psychological, and social changes that are least concerned and in some cases swept aside. In the early postpartum period, multiple challenges are faced by a mother such as physical recovery, hormonal imbalance, disturbance of sleep, and care (feeding) of the newborn. Despite the critical role of 4th-trimester care for maternal and infant well-being, most women do not have proper care as the visits to healthcare facilities are poorly attended and do not sufficiently address maternal concerns.[25] Therefore, most of the practicing obstetricians and the American College of Obstetrics and Gynecology (ACOG) recommend that medical professionals view postpartum care through the lens of maternal health. The mother must be provided with sufficient nutritional intake to their nutritional demand during the early postpartum period. The 4th trimester should be considered equally significant as the period of pregnancy and lactation.[26]

6. Nutritional Requirements of Lactating Mother (protein requirements in lactation)

According to the WHO expert committee, the optimal daily milk output of the mother's milk is estimated to be 850 ml. The effect of maternal nutrition during lactation (about 80% of energy, 50% of proteins and 30% of the calcium) is converted into the milk to the newborn.[13] In lactating women, during exclusive breastfeeding, habitual protein intake should be increased, if breast milk represents a substantial proportion of the infant's diet.[27]

Lactation provides 600 Kcal. 10.2 g protein, 290 mg calcium, 0.25 to 3.1 mg iron, 420 mcg Vitamin A, 22 to 44 mg ascorbic acid, 1.6 mg niacin, 0.52 mg riboflavin, 0.12 mg thiamine, 9.0 mcg folic acid, and 0.2 mcg vitamin B12.

Energy and proteins

During lactation, the mother requires an additional intake of energy (at least 550 kilocalories more). During the first 6 months of lactation and for the next 6 months, additional energy 400 kilocalories per day must be supplemented. Protein requirement is at its highest when lactation reaches its maximum, and the nursing mothers needs about 20–30 g/day of protein over and above her normal requirements.[16]

According to the ICMR and NIN, the recommended daily increment in protein intake in lactating women is about 20–30 g/day during lactation.

Minerals

Table 1. Recommended dietary allowances in Indian women (macronutrients, vitamins, and minerals)

Nutrient	Non-pregnant	Pregnant	Lactation
Energy (Kcal/d)	2850	3200	3450
Protein (g/d)	55	78	74
Calcium (mg/d)	600	1200	1200
Iron (mg/d)	21	35	21
Vitamin A (µg/d)	600	800	950
Ascorbic acid (mg/d)	40	60	80
Folate (mg/d)	200	500	300
Niacin (mg/d)	16	18	20
Riboflavin (mg/d)	1.7	2.0	2.1
Thiamine (mg/d)	1.4	1.6	1.9
Vitamin B6 (mg/d)	2.0	2.5	2.5
Vitamin B12 (µg/d)	1	1.2	1.5
Zinc (mg/d)	10	12	12
Iodine (mcg/d)	150	220	290
Magnesium (mg/d)	310	310	310

Minerals such as iron, iodine zinc, selenium, magnesium, and other minerals play an important role during pregnancy and lactation. Therefore, it has been recommended to be supplemented during pregnancy and lactation.[5]

Vitamins

The additional requirement of vitamin A during lactation is calculated based on the amount secreted in milk, which is 350 mcg of retinol per day. Vitamin D requirements may be higher during lactation and an additional need of 40 mg vitamin C has been calculated based on vitamin C secreted in milk in an average yield of 850 ml/day in a well-nourished mother. Similarly, additional intake of vitamin B6, folic acid and vitamin B12 are recommended to the tune of 0.5 mg, 50 mcg, and 0.5 mcg respectively.[16]

The ICMR Nutrition Expert Committee has estimated that the average amount of milk secreted by lactating mothers in India to be 600 ml. Accordingly, the nutrition requirement of the lactating women (weighing 55 kg) in India is according to that provided in Table 1.[16]

Role of specific vitamins and minerals during pregnancy and lactation

Calcium

Additional calcium is needed for the growth and development of bones as well as teeth of the fetus. ICMR recommended a total of 1.2 g of calcium during pregnancy which takes care of the total calcium needs of the mother and the additional needs of pregnancy.[28] During lactation, an intake of 1.2 g/d is recommended to be continued as a lactating woman produces about 750 ml of milk daily, which represents about 280 mg of calcium (7.0 mmol).[29]

ICMR recommends a total of 1.2 g of calcium intake in pregnancy and to continue with 1.2 g during lactation.

Vitamin D

The requirement for vitamin D also may be higher during pregnancy when calcium metabolism is under physiological stress.[16] Vitamin D deficiency is common during pregnancy, especially in high-risk groups like vegetarians, women living in cold climates, and women with darker skin. If vitamin D deficiency is discovered during pregnancy, then supplements (1000–2000 IU per day) can be considered.[5]

Zinc

Zinc has an important role to play in pregnancy, as it is involved in the synthesis of nucleic acids – DNA and

RNA which is significant in the process of reproduction, see table 1 for daily intake recommendation.[5]

Iron

Iron is needed for the increasing volume of blood and other tissues formed during the development of a fetus. The store for iron is built during the prenatal period as milk, which is the main food of infants during the first three to four months, is deficient in iron. It is now a common practice for the doctor to give expectant mothers a prescription for an iron salt. The recommended dietary iron is made considering an 8% absorption, which meets the approximate requirement of 3.4 mg per day during pregnancy and lactation.[5]

Iodine

If the mother's iodine intake is low, the infant may suffer from cretinism, a disease characterized by retarded physical and mental development. In pregnancy, the iodine requirement is enhanced.[5]

Magnesium

Several studies on pregnancy diet have shown that magnesium intake is often less than the recommended amount. Magnesium supplementation has shown to reduce preterm births, number of cases of maternal hospitalization, predelivery bleeding and LBW newborns.[30]

Other essential vitamins

- The additional intake of thiamine 0.2 mg, riboflavin 0.2 mg, and nicotinic acid 2 mg has been recommended per 1000 kcal respectively, correlating with the increased calorie intake.[16]
- Increased energy allowance will provide the increased B complex vitamins.[16]
- An increased level of vitamin B6 and folic acid is recommended.[16]

It is difficult to provide these amounts of nutrients through food and the additional needs may have to be met through supplements of medicinal folate. Also, the information about the additional needs of vitamin B12 in pregnancy is limited. However, based on various studies, ICMR has suggested an intake of vitamin B12 1.5 mg/day during pregnancy.[16]

7. Ideal formulation containing PVMs in pregnancy and lactation

Optimum protein, adequate vitamins and minerals intake during pregnancy and lactation is associated with the overall growth and development of the newborn till the age of 5 years. High protein intake in early pregnancy may lead to an in utero effect on the offspring's body composition with a higher weight initially at birth but slower growth rates into childhood. Hence, ideal optimum protein intake must be considered.[1] As per earlier specifications regarding protein intake, the ideal formulation must contain the recommended quantity of PVMs.[4,16]

Clinical evidence supporting the role of supplementing PVMs in pregnancy and lactation

Micronutrients and trace elements have a significant impact on the health of mother and fetus. During pregnancy, deficiency of micronutrients may cause complications like anemia, hypertension, impairing fetal function, development, and growth. Role of various micro, macronutrients and trace elements during pregnancy and lactation is given in Table 2.[26]

Table 2. Role of various micronutrients, macronutrients, and trace elements during preconception, pregnancy and lactation[3,4,17,26,30–37]

Nutrient	Impact on a nutrient deficiency on mother and fetus
Energy	To prevent poor pregnancy outcomes associated with both insufficient and excessive gestational weight-gain, adequate maternal energy intake is important.[3]
Proteins	Protein is involved in both structural (tissues, muscles, bones) and functional (enzymes, protein transport, hormones) biological roles. A 15% and 25% absolute increase in protein synthesis occurs during the second and third trimesters vs. early pregnancy and non-pregnant women.[3]
Carbohydrates	The glycemic index (GI) quantifies glycemic responses induced by carbohydrates from different foods. High GI foods lead to a sharp rise in blood glucose levels which decreases rapidly.[3]
Preconception recommendations	
Folic acid	Folic acid supplementation is very important during the pre and periconception period as it reduces the risk of congenital malformations. Deficiency in folate during pregnancy may lead to serious fetal complications such as neural tube defects.[4] Accumulation of homocysteine is associated with folate deficiency, resulting in an increased risk of adverse outcomes including preeclampsia and fetal anomalies.[3] Hence, it is recommended an intake of 500 mcg (0.5 mg) folic acid supplementation is advised preconceptionally and throughout pregnancy for women with a history of congenital anomalies (neural tube defects, cleft palate).[4]

Nutrient	Impact on a nutrient deficiency on mother and fetus
Vitamin B12	Vitamin B12 deficiency is associated with adverse maternal and neonatal outcomes such as developmental anomalies, spontaneous abortions, preeclampsia, and LBW. Therefore, adequate vitamin B12 status periconceptionally is very important. It also has a fundamental role in neural myelination, brain development, and growth.[31]
Recommendations during pregnancy and lactation	
Essential fatty acids (fats)	Fats are a concentrated source of energy that provides 9 Kcal/g and is made up of fatty acids in different proportions.[4] Omega-3 fatty acids particularly docosahexaenoic fatty acid (DHA) is widely identified to impact fetal and infant neurodevelopment. The role of DHA in brain development and its inefficient synthesis from the essential alpha-linolenic acid (ALA) has led to the recommended intake of eicosapentaenoic acid (EPA) and DHA in pregnancy and lactation by the Dietary Guidelines for Americans. Also, the importance of EPA and DHA in infant development has been recognized widely that led to the recommendations for pregnant and lactating women from many regulatory bodies and medical/scientific societies.[32,33]
Inositol	An isomer of inositol, myo-inositol, one of the intracellular mediators of the insulin signal and is correlated with insulin sensitivity in type 2 diabetes. Myo-inositol is reported to play an important role in the mother and fetus, in preventing gestational diabetes.[34]
Vitamin B group (B1, B2, B3, B6, B9, and B12)	Important for enhancing the immune system as well as reducing the plasma concentration of homocysteine. Pre-eclampsia, premature birth, and LBW are found to be associated with elevated maternal plasma homocysteine levels as a result of vitamin B deficiency.[31]
Vitamin A	Supplementation of vitamin A may elevate hemoglobin concentrations by about 4 g/L in maternal populations with deficiency. Vitamin A intake of 800 µg daily is recommended during pregnancy. Vitamin A is found to be at optimum levels in breast milk. However, adequate maternal dietary vitamin A is recommended in the maintenance of adequate levels in the breast milk.[31]
Vitamin E	Protects polyunsaturated fatty acid from free radical damage.[31]
Vitamin C	Stimulates better absorption of iron and in turn, reduces the risk of maternal anemia. It also guards the body against injurious free radicals as an antioxidant. The recommended daily intake of vitamin C in pregnancy is 60 mg/day.[31]
Vitamin D	Helps to absorb calcium and phosphorous from dietary intakes, which are required for stimulating skeleton formation of the fetus.[31]
Calcium	Calcium is essential during pregnancy and lactation. Calcium supplementation helps in: • Reducing the risk of pregnancy-induced hypertension (PIH) and a decrease in circulating lead.[31] • Proper formation, growth, and development of bones and teeth in the fetus.[4] • Maintenance of fetal bone mineralization. [31] • Secretion of breast milk rich in calcium.[4] • Prevention of osteoporosis in the mother.[4]
Magnesium	In pregnancy, magnesium supplementation may be beneficial as hypomagnesemia may lead to hypertension, preeclampsia and preterm birth in pregnancy.[17]
Phosphorus	Regulates acid-base balance in the bloodstream and activate catalytic proteins.[32]
Biotin	Biotin supplementation helps to overcome biotin deficiency which is associated with increased risk of birth defects. Biotin deficiency was found both in the early (first trimester) and late (third trimester) stages of pregnancy.[35,36]
Iron	Adequate iron is required from conception, throughout the pregnancy, and during lactation. Iron supplementation may be helpful to overcome the iron deficiency in pregnancy that may cause preterm delivery and maternal anemia. Also, iron deficiency during lactation is associated with mental retardation. Hence, iron should be supplemented and the recommended daily iron intake for pregnant women is 27 mg/day.[26]
Iodine	Plays a key role in fetal and neonatal growth and development. Severe iodine deficiency may result in abortion or stillbirth, congenital anomalies, neurological cretinism, or mental retardation with deafness, spastic diplegia, squint, and myxoedematous cretinism. Iodine is essential for thyroid hormone synthesis.[26]
Zinc	Zinc helps in maintaining the structural integrity of proteins and regulate gene expression.[26]
Manganese	Manganese plays an important role in the process of pregnancy and normal fetal development.[30]
Molybdenum	Activates enzymes involved in the metabolism of sulfur-containing amino acids and nitrogen-containing compounds contained in deoxyribonucleic acid (DNA and ribonucleic acid (RNA).[30]
Selenium	It has an antioxidant property as well as a role in cellular function and muscle maintenance.[26]
Chromium	For the normal functioning of the insulin hormone, chromium is needed. Chromium supplements may be beneficial in regulating glucose levels in pregnant women with gestational diabetes.[30]
Copper	Copper is a vital cofactor of antioxidant enzymes. In mother and fetus, these enzymes play a key role in removing pregnancy oxidative stress.[30]
Taurine	Taurine supplementation may help to prevent taurine-deficiency in the mother that may cause growth retardation, impaired perinatal development of central nervous system, and pancreas in the offspring.[37]

Table3. Clinical evidence suggesting the role of macro and micronutrients in pregnancy and lactation.[8,13,35,38–51]

Study	Study population	Intervention	Clinical outcomes
Energy			
Meta-analysis	Overweight women or who exhibited excessive gestational weight-gain	Energy/ protein restriction	Significantly reduced weekly maternal weight-gain and mean birth weight. Among all trials, 13 trials (n=4665) showed modest increase in maternal weight-gain, mean birth weight, and a substantial reduction in the risk of small-for-gestational-age (SGA). Significant reduction in the risks was also observed for stillbirth and neonatal death.[38]
Protein/energy			
Literature review	Pregnant women with energy or protein deficit	Protein/ energy supplement (up to 20% energy as protein)	Improvement in fetal growth increased the birth weight (by 95–324 g) and height (by 4.6–6.1 mm), and decrease in the percentage of LBW (by 6%) was observed.[13]
Systematic review and meta-analysis (7 studies)	Undernourished pregnant women (low- and middle-income countries on child growth)	Balanced protein energy supplementation	Pooled results indicate that the intervention had a significant moderate effect on birth weight [RCT=7, intervention: n=1228; control: n=1139; difference=0.20 [95% confidence interval (CI): 0.03–0.38, p=0.02].[39]
Carbohydrate			
Systemic literature review	Pregnant women	Low glycemic index (GI) food	In healthy women, low GI diets reduced the risk of large-for-gestational-age (LGA) infants.[40]
	Women with gestational diabetes mellitus	Low GI diet	Low GI diets reduced the amount of insulin required to maintain optimal glycemic control.[40]
Myo-inositol			
Systematic reviews	Pregnant women	Myo-inositol, alone or in a combination preparation	Supplementation with myo-inositol reduced the incidence of gestational diabetes vs. control (risk ratio (RR) 0.43, 95% CI 0.29 to 0.64; three trials; n=502 women).[41]
Maternal nutritional supplementation [protein, fat, carbohydrate, and a variety of micronutrients (calcium, iron, vitamin A, zinc, vitamin E, vitamin C, and B-vitamins (B1, B2, B3, B6, B9, B12)]			
Prospective	Pregnant women (26–29 weeks gestation till 12 weeks post-partum	Maternal nutritional supplemen-tation vs. standards of care.	A significantly higher birth weight (p=0.0312), birth weight-for-age (p=.0141), birth head circumference-for-age (p=0.0487), and head circumference-for-age z-score (p=0.0183) development during postnatal period observed in the intervention group vs. control.[42]
Multi-micronutrient supplementation (Vitamin A, vitamin B1, vitamin B6, folic acid, zinc, iron, copper)			
A meta-analysis	Pregnant women	Prenatal supplemen-tation with multi-micronutrients on pregnancy outcomes	A significant reduction in the risk of LBW was observed vs. placebo (RR 0.81, 95% CI 0.73–0.91) or iron-folic acid supplementation (RR 0.83, 95% CI 0.74–0.93). In multi-micronutrient group, birth weight was significantly higher vs. mothers received iron-folic acid supplementation (weighted mean difference 54 g, 95% CI 36 g–72 g).[43]
Folic acid			
Systemic review	Pregnant women	Folic acid with micronutrient vs. placebo	Folic acid improved mean birth weight (mean difference (MD) 135.75, 95% CI 47.85 to 223.68) significantly reduced the incidence of megaloblastic anemia (RR 0.21, 95% CI 0.11–0.38, n= 3839).[44]
Systemic review	Peri-conceptional	folate supplemen-tation alone, or in combination with other vitamins and minerals	Folic acid, alone or in combination with vitamins and minerals vs. no interventions/ placebo or vitamins and minerals without folic acid is found to prevent neural tube defects (NTDs) (risk ratio (RR) 0.28, 95% CI 0.15 to 0.52).[45]
Vitamin A			
Systemic review	Postpartum women	vitamin A	Supplementation in the puerperium increases the concentrations of serum retinol and breast milk.[46]
Vitamin K			
Systematic review and meta-analysis	Pregnant women	Vitamin K + nutrients vs. placebo	In the intervention group an increase in maternal plasma vitamin K was observed (MD 2.46, 95% CI 0.98–3.93; p=0.001).[47]
Vitamin D			
Meta-analysis (24 trials, n=5405).	Pregnant women	Vitamin D supplementation – prenatal and during pregnancy.	The intervention was safe. Vitamin D reduced SGA with a RR of 0.72 (95% CI: 0.52 to 0.99; n=898; 6 trials; I_2 0%), increased birth weight by 75.38 g (95% CI: 22.88 to 127.88; n=4087; 17 trials; I_2 44%), Reduced fetal or neonatal mortality (RR: 0.35; 95% CI: 0.15 to 0.80). It also Increased serum calcium levels by 0.19 mg/dL (95% CI: 0.003 to 0.38 mg/dL; n=1007; 9 trials; I_2 74%). Increased Apgar scores at 1 min by 0.09 (95% CI: 0.01 to 0.17; n=670; 4 trials I_2 40%) and at 5 min by 0.08 (95% CI: 0.02 to 0.14; n=668; 4 trials; I_2 13%).[48]
2 Meta-analysis	Pregnant women at risk of pre-eclampsia		Vitamin D supplementation reduces the risk of pre-eclampsia [RR:0.41 (95% CI: 0.22 to 0.78)) and 0.47 (95% CI: 0.24 to 0.89), respectively].[49,50]
Study	**Study population**	**Intervention**	**Clinical outcomes**

Vitamin B_{12}			
RCT	Pregnant and lactating women (183 women were randomly assigned to vitamin B12 and 183 to receive placebo).	Vitamin B12 or placebo was given to women from early pregnancy, (<14 weeks gestation), through 6 weeks postpartum.	In vitamin B12 supplemented women vs. placebo, a significantly higher plasma vitamin B-12 concentrations at both the second (median vitamin B12 concentration: 216 vs. 111 pmol/L, p<0.001) and third (median: 184 vs. 105 pmol/L, p<0.001) trimesters was observed. The Median breast milk vitamin B12 concentration, at 6-week postpartum, was high in vitamin B12 supplemented women vs. placebo group (136 pmol/L vs. 87 pmol/L) (p<0.0005). Median plasma vitamin B12 concentration in the infant (6-week of age) born to supplemented women was 199 pmol/L vs. 139 pmol/L in the placebo group (p=0.01).[8]
Calcium supplementation			
A Meta-analysis (13 randomized trials, n=15,730 pregnant women)	Pregnant women	Calcium supplementation vs. placebo or no calcium	Calcium reduced high BP vs. placebo (12 trials, 15,470 women: risk ratio (RR) 0.65, 95% CI 0.53 to 0.81; I^2=74%) and showed a significant reduction in the risk of pre-eclampsia, specifically in women with low calcium diets (8 trials, 10,678 women: average RR 0.36, 95% CI 0.20 to 0.65; I^2=76%) and women at high risk of pre-eclampsia (5 trials, 587 women: average RR 0.22, 95% CI 0.12 to 0.42; I^2=0%). The risk of preterm birth was also reduced in calcium group (11 trials, 15,275 women: RR 0.76, 95% CI 0.60 to 0.97; I^2=60%). Maternal death or serious morbidity (4 trials, 9732 women; RR 0.80, 95% CI 0.65 to 0.97; I^2=0%) were also reduced.[51]
Biotin			
Randomized controlled trial (26 pregnant women with increased 3-HIA excretion)	10 women, early pregnancy; 6–17 week gestation) and 16 women, late pregnancy; 21–37 week gestation).	Biotin (300 µg/d for 14 days; 5 EP, 8 LP) vs. placebo (5 EP, 8 LP).	3-hydroxyisovaleric acid (3-HIA) excretion decreased (p <0.006) by 11.7 ± 3.6 mmol/mol creatinine (mean ± SEM) in the women who received biotin supplements, whereas 3-HIA excretion increased by 1.6 ± 0.6 mmol/mol creatinine in the women who received placebo. Marginal biotin deficiency occurs frequently in the 1st trimester that raises the concern about potential human teratogenicity. Biotin reduces the risk of teratogenicity.[35]

8. Recommendation for supplementing PVMs during pregnancy and lactation

- Protein intake in non-pregnant state is 46 g/d while in pregnancy it is recommended to be increased to 60 g/day. In other words, this increase does reflect a change to 1.1 g of protein/kg/d during pregnancy from 0.8 g of protein/kg/d for non-pregnant states.
- Folic acid supplementation in preconception care and periconceptional intervention may be beneficial in improving maternal nutritional status and neonatal health outcomes.
- To prevent poor pregnancy outcomes associated with both insufficient and excessive gestational weight-gain, adequate maternal energy intake is important.
- During lactation, the demand for protein is increases based on the proteins secreted in breast milk.
- EPA and DHA intake is also very important in pregnancy and lactation. It is helpful in physical development and growth and also it is widely recognized to impact fetal and infant neurodevelopment.
- Calcium supplementation helps in reducing the risk of PIH in mothers and maintenance of bones and teeth in the offspring/fetus/neonates.
- The ICMR recommends a total of 1.2 g/d of calcium intake during pregnancy and to continue the same during lactation.
- The ICMR recommends increased iron intake during pregnancy. An intake of 35 mg/day is recommended in comparison to 21 mg/day in non-pregnant women.
- The ICMR recommendation for iodine, zinc, and all other minerals is also increased during pregnancy and lactation. For iodine 220 mg/d intake in pregnancy and 290 mg/d during lactation. For zinc, an intake of 12 mg/d is recommended during pregnancy and lactation.
- An additional intake of B-complex vitamins is required correlating with the increased calorie intake. There may be a higher demand for vitamin D during pregnancy when calcium metabolism is under physiological stress.
- The fourth trimester is marked by significant biological, psychological, and social changes which are neglected and in some cases swept aside.

- The 4th trimester should be considered equally significance as the period of pregnancy and lactation.
- The first 6 months of lactation and for the next 6 months after lactation, additional 400 kilocalories energy is required. Protein requirement is at its highest during lactation, as it reaches to its maximum requirement. Therefore the nursing mother needs about 20–30 g of protein over and above her normal requirements.
- The consequences for fetal and infant health include increased risk of fetal, neonatal, and infant death. There is also a risk of intrauterine growth retardation, LBW, prematurity, birth defects, cretinism, brain damage, and increased risks of infection.
- An ideal formulation containing optimum protein intake, adequate micronutrients (various vitamins and minerals) must be considered during pregnancy and lactation as it effects the overall growth and development of the newborn till the age of 5 years.
- Based on the provided evidence supporting the role of PVMs in pregnancy and lactation (table 2), an ideal formulation should include– Energy, Protein, Carbohydrate, Fat, Inositol, Gamma Linoleic Acid, Taurine, Colostrum, Vitamin C, Vitamin E, Vitamin B2, Vitamin B1, Vitamin A, Vitamin B6, Folic Acid, Biotin, Vitamin K, Vitamin D, Vitamin B12, Calcium, Phosphorus, Magnesium, Iron, Zinc, Copper, Manganese, Iodine, Chromium, Molybdenum, and Selenium.
- Exclusive breastfeeding is recommended for the first 6 months of life and is associated with decreased incidence of infections and chronic diseases.

References

1. Geraghty AA, O'Brien EC, Alberdi G, et al. Maternal protein intake during pregnancy is associated with child growth up to 5 years of age, but not through insulin-like growth factor-1: findings from the ROLO study. Br J Nutr. 2018;120(11):1252–1261. **2.** Bloomfield FH, Spiroski A-M, Harding JE. Fetal growth factors and fetal nutrition. Semin Fetal Neonatal Med. 2013;18(3):118–123. **3.** Mousa A, Naqash A, Lim S. Macronutrient and micronutrient intake during pregnancy: An overview of recent evidence. Nutrients. 2019;11(2):443. **4.** Dietary guidelines for Indians - A manual. National Institute of Nutrition. Indian Council of Medical Research. Available at: http://ninindia.org/DietaryGuidelinesforNINwebsite.pdf. Accessed 16 Sept 2019. **5.** Kominiarek MA, Rajan P. Nutrition recommendations in pregnancy and lactation. Med Clin North Am. 2016;100(6):1199–1215. **6.** Wilson Rl, Gummow JA, McAninch D, et al. Vitamin and mineral supplementation in pregnancy: evidence to practice. Journal of Pharmacy Practice and Research. 2018; 48:186–192. **7.** Pena-Rosas JP, De-Regil LM, Garcia-Casal MN, Dowswell T. Daily oral iron supplementation during pregnancy. Cochrane Database Syst Rev. 2015;(7):CD004736. **8.** Duggan C, Srinivasan K, Thomas T, et al. Vitamin B-12 supplementation during pregnancy and early lactation increases maternal, breast milk, and infant measures of vitamin B-12 status. J Nutr. 2014;144(5):758–64. **9.** Herrera E, Ortega H. "Metabolism in normal pregnancy", in Di Renzo G.C. (ed.) Textbook of diabetes and pregnancy. London: Informa healthcare, pp. 25–34, 2008. **10.** Elango R, Ball RO. Protein and amino acid requirements during pregnancy. Adv Nutr An Int Rev J. 2016;7(4):839S–844S. **11.** Bhutta ZA, Ahmed T, Black RE, et al. What works? Interventions for maternal and child undernutrition and survival. Lancet. 2008;371(9610):417–40. **12.** Barros FC, Bhutta ZA, Batra M, et al. Global report on preterm birth and stillbirth (3 of 7): Evidence for effectiveness of interventions. BMC Pregnancy Childbirth. 2010;10(1):S3. **13.** Liberato SC, Singh G, Mulholland K. Effects of protein energy supplementation during pregnancy on fetal growth: A review of the literature focusing on contextual factors. Food Nutr Res. 2013;57. **14.** Vaiserman A, Lushchak O. Prenatal malnutrition-induced epigenetic dysregulation as a risk factor for type 2 diabetes. Int J Genomics. 2019;2019:1–11. **15.** Gernand AD, Schulze KJ, Stewart CP, et al. Micronutrient deficiencies in pregnancy worldwide: Health effects and prevention. Nat Rev Endocrinol. 2016;12(5):274–89. **16.** Nutrition during pregnancy: Part I weight-gain: Part II nutrient supplements. Institute of Medicine (US) Committee on Nutritional Status During Pregnancy and Lactation. Washington (DC): National Academies Press (US); 1990. **17.** Borazjani F, Angali KA, Kulkarni SS. Milk and protein intake by pregnant women affects growth of fetus. J Health Popul Nutr. 2013;31(4):435–45. **18.** Societa di Nutrizione Umana (SINU) LARN—Livelli di Assunzione di Riferimento di Nutrienti ed Energia per la Popolazione Italiana. SICS; Milano, Italy: 2014. IV Revisione. pp. 1–655. **19.** Truchet S, Honvo-Houeto E. Physiology of milk secretion. Best Pract Res Clin Endocrinol Metab. 2017;31(4):367–384. **20.** Verd S, Ginovart G , Calvo J, et al. Variation in the protein composition of human milk during extended lactation: A narrative review. Nutrients. 2018;10(8). pii:E1124. **21.** Bzikowska-Jura A, Czerwonogrodzka-Senczyna A, Olędzka G, et al. Maternal nutrition and body composition during breastfeeding: Association with human milk composition. Nutrients. 2018;10(10). pii: E1379. **22.** Bravi F, Wiens F, Decarli A, et al. Impact of maternal nutrition on breast milk composition: A systematic review. Am J Clin Nutr. 2016;104(3):646–62. **23.** Nutrition during lactation. Committee on nutritional status during pregnancy and lactation, Institute of Medicine. 1991; ISBN: 0-309-53767-3, 326 pages. Available from the National Academies Press at: http://www.nap.edu/catalog/1577.html. Accessed 16 Sept. **24.** Tully KP, Stuebe AM, Verbiest SB. The fourth trimester: a critical transition period with unmet maternal health needs. Am J Obstet Gynecol. 2017;217(1):37–41. **25.** Talai Rad N, Ritterath C, Siegmund T, et al. Longitudinal analysis of changes in energy intake and macronutrient composition during pregnancy and 6 weeks post-partum. Arch Gynecol Obstet. 2011 Feb;283(2):185–90. **26.** Lim CE, Yii MF, Cheng NC, Kwan YK. The role of micronutrients in Pregnancy. Aust Fam Physician. 2009;38(12):980–4. **27.** Marangoni F, Cetin I, Verduci E, et al. Maternal diet and nutrient requirements in pregnancy and breastfeeding. An Italian consensus document. Nutrients. 2016;8(10). pii:E629. **28.** Nutrition and health education. School of open learning. SM-1. Lesson 10: Nutrition during pregnancy and lactation. Available at: https://sol.du.ac.in/mod/book/view.php?id=1422&chapterid=1288. Accessed 16 Sept 2019. **29.** WHO. Vitamin and mineral requirements in human nutrition. Second edition. World Health Organization and Food and Agriculture Organization of the United Nations. 2004. **30.** Khayat S, Fanaei H, Ghanbarzehi A. Minerals in pregnancy and lactation: A review article. J Clin Diagn Res. 2017;11(9):QE01–QE05. **31.** Finkelstein JL, Layden AJ, Stover PJ. Vitamin B-12 and perinatal health. Adv Nutr. 2015;6(5):552–563. **32.** van Goor SA, Dijck-Brouwer DA, Erwich JJ, et al. The influence of supplemental docosahexaenoic and arachidonic acids during pregnancy and lactation on neurodevelopment at eighteen months. Prostaglandins Leukot Essent Fatty Acids. 2011;84(5-6):139–46. **33.** Devarshi PP, Grant RW, Ikonte CJ, Mitmesser SH. Maternal omega-3 nutrition, placental transfer and fetal brain development in gestational diabetes and preeclampsia. Nutrients. 2019;11(5). pii:E1107. **34.** Thomas M, Weisman SM. Calcium supplementation during pregnancy and lactation: effects on the mother and the fetus. Am J Obstet Gynecol. 2006;194(4):937–45. **35.** Mock DM, Quirk JG, Mock NI. Marginal biotin deficiency during normal pregnancy. Am J Clin Nutr. 2002;75(2):295–9. **36.** Mock DM. Marginal biotin deficiency is common in normal human pregnancy and is highly teratogenic in mice. J Nutr. 2009;139(1):154–157. **37.** Aerts L, Van Assche FA. Taurine and taurine-deficiency in the perinatal period. J Perinat Med. 2002;30(4):281–6. **38.** Kramer MS, Kakuma R. Energy and protein intake in pregnancy. Cochrane Database Syst Rev. 2003;(4):CD000032. **39.** Stevens B, Buettner P et al. The effect of balanced protein energy supplementation in undernourished pregnant women and child physical growth in low- and middle-income countries: a systematic review and meta-analysis. Matern Child Nutr. 2015;11(4):415–32. **40.** Louie, JCY, Brand-Miller JC, et al. Glycemic index and pregnancy: A systematic literature review. J. Nutr. Metab. 2010, 2010, 282464. **41.** Crawford TJ, Crowther CA, et al. Antenatal dietary supplementation with myo-inositol in women during pregnancy for preventing gestational diabetes. Cochrane Database Syst Rev. 2015;(12):CD011507. **42.** Huynh DTT, Tran NT et al. Impact of maternal nutritional supplementation in conjunction with a breastfeeding support program on breastfeeding performance, birth, and growth outcomes in a Vietnamese population. J Matern Fetal Neonatal Med. 2018;31(12):1586-1594. **43.** Shah PS, Ohlsson A; Knowledge Synthesis Group on Determinants of Low Birth Weight and Preterm Births. Effects of prenatal multimicronutrient supplementation on pregnancy outcomes: a meta-analysis. CMAJ. 2009;180(12):E99–E108. **44.** Lassi ZS, Salam RA et al. Folic acid supplementation during pregnancy for maternal health and pregnancy outcomes. Cochrane Database Syst Rev. 2013 Mar 28;(3):CD006896. **45.** De-regil LM, Pena-Rosa JP et al. Effects and safety of periconceptional oral folate supplementation for preventing birth defects. Cochrane Database Syst Rev. 2015;(12):CD007950. **46.** Soares MM, Silva MA et al. Efect of vitamin A supplementation: a systematic review. Cien Saude Colet. 2019;24(3):827-838. **47.** Shahrook S, Ota E, Hanada N, Sawada K, Mori R. Vitamin K supplementation during pregnancy for improving outcomes: a systematic review and meta-analysis. Sci Rep. 2018;8(1):11459. **48.** Bi WG, Nuyt AM et al. Association between vitamin D supplementation during pregnancy and offspring growth, morbidity, and mortality: A systematic review and meta-analysis. JAMA Pediatr. 2018;172(7): 635–645. **49.** Fu ZM, Ma ZZ et al. Vitamins supplementation affects the onset of preeclampsia. J Formos Med Assoc. 2018;117(1):6-13. **50.** Khaing W, Vallibhakara SA et al. Calcium and vitamin D supplementation for prevention of preeclampsia: A systematic review and network meta-analysis. Nutrients. 2017;9(10):1141. **51.** Hofmeyr GJ, Lawrie TA et al. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems (Review) .Cochrane Database Syst Rev. 2014;(6):CD001059.

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