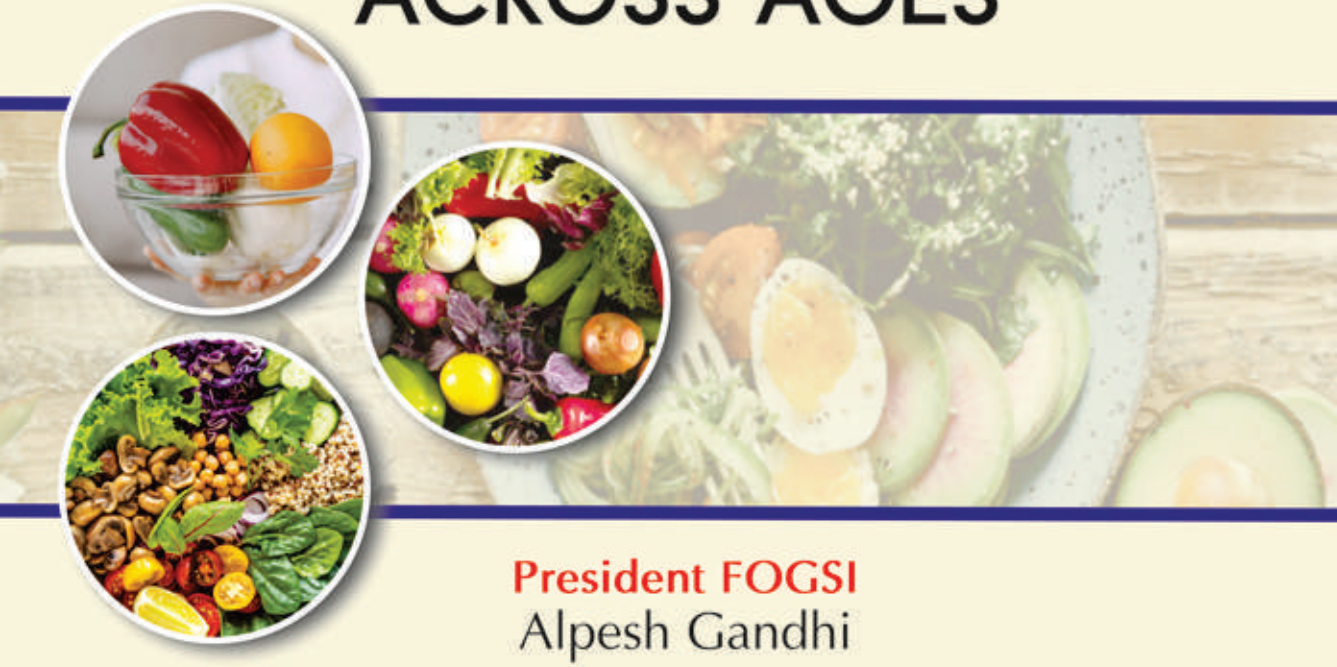
FOGSI FOCUS
NUTRITION IN WOMEN: ACROSS AGES



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New Delhi-110034, India
Phone: +91-11-42637878
E-mail: info@evangelpublications.com
Webstie: www.evangelpublications.com

ISBN:

Printed in India

Published and exclusively distributed by EVANGEL PUBLISHING

Foreword

It gives me immense pleasure to write a foreword for this endeavor of the FOGSI Food, Drugs and Medicosurgical Equipment Committee "**FOGSI Focus—Nutrition in Women: Across Ages"**.

Academics and evidence based practice has been one of the priorities for FOGSI. This Focus is a step forward in working towards the mission. As an endeavor of FOGSI, this Focus summarizes for the readers, the essential and latest evidence based developments in the field of nutrition in lifecycle of a woman. The topics have been aptly chosen to cater to all phases of a woman's life. It is comprehensive in its coverage as an amalgamation of latest topics related to nutrition in adolescence, reproductive life, pregnancy and menopause which are often neglected and overshadowed by other disease processes in a women's life. Creating best awareness about this all important topic of nutrition is a step forward in the way of "Women Empowerment" as healthy women can contribute better towards personal and professional developments.

I congratulate Dr Alpesh Gandhi and Dr T Ramani Devi to bring forward this concept of women's health. The editors Dr Vidya Thobbi and Dr Monika Gupta and all contributors have worked hard to do justice to the latest evidence-based recommendations on pertinent topics on nutrition. This will definitely benefit the practicing clinicians, residents as well as faculty in Obstetrics and Gynaecology.

I am sure the contents will help the readers in augmenting their clinical knowledge.

CN Purandare

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Special Message

Dear All!

Journey to healthy life is your lifestyle & diet is the main component of this.

In 4 walls of Medical College the modern medicine Doctors are not taught about Nutrition & Diet. Newspapers, magazines these days are full of articles on diet and dieting which tells what is healthy, what is not, whether you should take fat or not. The information presented can often be confusing at best and plainly unscientific at worst

While working as teacher with Indian doctors, I feel single most important factor which is lacking in their training is about ideal nutrition. India is poor, overpopulated and deeply religious country with diverse food practices to keep local people healthy & happy.

If you want to become good to great doctor-you have to show the mirror of ideal nutrition and diet to your patients. That is why a Doctor should study in depth about nutrition and guide the patients about diet in diseases & age wise, otherwise time is not far away when the dieticians will take over as doctors.

I congratulate the editors, Dr Vidya Thobbi & Dr Monika Gupta and all the authors for bringing out an excellent FOGSI focus which encourages gynaecologists to council patients on diet in their journey to healthy life. They also emphasize that nutritional intervention can make great difference in becoming healthy

Sharda Jain
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President Message

Dear FOGSIANs

FOGSI believes that Nutrition is a basic human need, a basic human right and a prerequisite for a healthy life. An adequate, well balanced diet with a wide range of nutrients combined with regular physical activity is a cornerstone of good health.

Better nutrition is directly related to improved health across lifespan, stronger immune systems, safer pregnancy and childbirth, lower risk of non-communicable diseases. Poor nutrition can lead to reduced immunity, increased susceptibility to disease, impaired physical and mental development, and reduced productivity.

Maternal malnutrition, before and in the pregnant state, is a worldwide problem with significant consequences, not only for survival and increased risk for acute and chronic diseases both in mother and child, but also for economic productivity of individuals in the societies and additional costs on the health system. Pre-pregnancy underweight and insufficient gestational weight gain are considered as individual risk factors for the occurrence of spontaneous interruption, preterm birth, fetal growth restriction, and hypertensive disorders, strongly associated with poorer perinatal outcome. Pre-conceptional care is essential and 1000 days needs to be extended to cover this period

Maternal pre-pregnancy obesity is a contributing factor in the etiology of poor maternal outcomes such as gestational diabetes, pregnancy-induced hypertension, risk of preterm birth, pre-eclampsia and eclampsia, venous thromboembolism, fetal macrosomia. Maternal obesity contributes to development of a number of negative maternal health outcomes. Higher rate of instrumental delivery and caesarean section, longer postpartum hospital stays than non-obese women.

It is FOGSI's vision is to work for Anaemia Mukt Bharat, promotion of breastfeeding, prevention of Non Communicable Diseases and safeguarding and prevention of maternal and neonatal mortality to achieve SDG for our country. We have worked for nationwide mass awareness and sensitization of community as well.

FOGSI believes that a proper, adequate, balanced diet with varied nutrition from conception, during intrauterine life to neonate, infant, adult age,

menopausal age and throughout life is essential for good health and wellbeing of everyone.

I congratulate **Dr Vidhya Thobbi**, chairperson & **Dr Monika Gupta**, North-Zone coordinator FOGSI Foods, Drugs and Instruments committee, for editing this valuable FOGSI FOCUS and all the authors for their valuable contributions. I hope it will help our members in their routine practice.

Please take care of yourself. Stay healthy, positive and safe.

Alpesh Gandhi
President, FOGSI

Vice President Message

Dear All,

It is my Privileged to present **FOGSI Focus—Nutrition in Women: Across Ages** as Vice President Incharge of Food, Drug and Medico Surgical Equipment Committee of FOGSI

FOGSI has been always inspiring and promoting, knowledge sharing in the field of Obstetrics and Gynaecology. This FOGSI FOCUS is dedicated to nutrition in varying aspects of Obstetrics and Gynaecology. First 1000 days of conception to post-partum is considered to be the most important period in the growth of the fetus and the new born. Most of the diseases which are seen in early child hood will have an impact upon later onset adult disease. So, by manipulating the diseases from the mother and the new born we can successfully create a healthy and a disease free future generation.

The incidence of infertility is on the rise, mostly because of the increase in the oxidative stress. This could very well be handled by manipulating the nutrition of the couple. Which can reduce the oxidative stress.

This FOGSI FOCUS covers varying topics on the important of nutrition.

I congratulate Prof. Dr. Vidya Thobbi, Chairperson Food, Drug and Medico Surgical Equipment Committee for being the main person behind such a beautiful FOGSI FOCUS.

I also congratulate the Dr. Monika Gupta for having work hard along with Prof. Dr. Vidya Thobbi, to bring out this beautiful FOGSI FOCUS on nutrition.

With best regards,

T Ramani Devi
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From Editors' Desk

Greetings to All !,

It gives us immense pleasure to present to you the "**FOGSI Focus—Nutrition in Women: Across Ages"**. We are grateful to Dr Alpesh Gandhi, President FOGSI and Dr T. Ramani Devi, Vice-President In-charge for entrusting us with this opportunity. Of course, this opportunity has come with a huge responsibility of keeping up with the standards of evidence based education and learning.

The theme of FOGSI for this year has been **"Safety first, for Indian women and for FOGSIANS"**. Keeping in line with this theme we are dedicating our focus to an important aspect of health of Indian women which is often neglected. Providing quality healthcare to our Indian women across all ages has always been the motive of all FOGSIANs. This is a small effort from us in the direction of women's health i.e. nutrition for her in all stages of her life.

On behalf of the editorial team I thank all the authors for their valuable contributions in covering important aspects of nutrition in women in their articles. We have tried to present to you, an exhaustive compendium of important topics in different categories like 'nutrition in Adolescence, PCOS, reproductive age group, pregnancy and lactation and also menopause'. The importance of essential components of diet like 'Proteins, Vitamins, Minerals and Probiotics' has been well highlighted through various chapters. Another topic covered here is 'Epigenetics of nutrition' which is comparatively a newer and lesser discussed concept.

We have also included the 'FIGO Nutrition Guidelines and Checklists' as a ready reckoner in the appendix section of the focus.

We hope that this FOGSI Focus is beneficial for both practitioners and academicians. We look forward for your suggestions and feedback to bring forth the best in future as well.

Happy Reading!

Vidya Thobbi
Monika Gupta
Editors

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Contents

Chapter 1

Adolescent Nutrition

Sampathkumari, Niranjana

Introduction

All individuals have two growth phases during their lifetime—at infancy and at adolescence. Hence, they require lot of nutrients like vitamins and minerals. A study in 2000 analyzed adolescent nutrition and found malnutrition is common among adolescents. It reported that while developing countries suffer from undernutrition, adolescents in developed countries are under social pressure for achieving a distorted body image. On the other end of spectrum obese adolescents grow up to have chronic diseases and burden the health care.[1]

Global nutrition report 2020 states India will miss global nutritional targets by 2025, which includes adolescent underweight, overweight, and obesity among other indicators.[2] The report says investing in nutrition gives a 16:1 benefit to cost ratio for low income and developing countries.

Why Is It Important

Adolescence is the period of growth and to support their growth, adequate nutrients are required. They are nutritionally vulnerable and deficiencies in adolescence cause problems in long-term health. India has about 253 million adolescents aged between 10–19 years, about 25% of total population, of which 40% girls and 18% boys are anemic.[3]

Proper nutrition ensures optimal growth. During growth spurt, between 9–11 years girls gain 24–26 cm and 11–14 years boys gain 27–29 cm in height. Undernutrition delays development of secondary sexual characters and pubertal changes by about 1 year in boys and 0.82 year in girls.[4]

Adolescents are not a homogenous group and require varied solution depending on their cultural, ethnic, and personal preferences. This period of transition to adulthood involves physical and psychological changes. Malnutrition can result in long–term health complications.

What Is Healthy Eating

Growth and development in puberty requires additional energy. This energy is to be provided from healthy foods. Healthy eating involves diet rich in fiber, with restricted salt intake, adequate fruits, and vegetables. Chicken and fish are healthy options for non-vegetarian diet over red meat. A survey has reported that adolescents tend to eat added sugars, saturated fatty acids, salt, carbonated drinks more than the required.[5]

Along with healthy eating, an active lifestyle should be maintained to ensure proper growth and development. At least 60 minutes of moderate intensity workout is recommended for an adolescent. This should include daily aerobic exercises and exercise to strengthen bones for 3 days a week, and exercises to build muscles for remaining 3 days.[6] This healthy lifestyle ensures they enter adulthood with good health and do not become burden of health care.

Composition of Food

Carbohydrates are the most important source of energy contributing to about 50–60% of total energy. NCEP recommendation states that only 30% of energy should be obtained from fat of which saturated fat should be <10%.[7] Protein requirement is determined by lean body mass, which provides 10–15% of total energy requirement. Dietary fiber intake should be 15.5–34.5 g/day for adolescent males and 16–28.5 g/day for adolescent females. Fluid is required to maintain hydration. Vitamins and other micronutrients are essential for normal body functioning. Iron is required to prevent anemia and heme sources are better than non-heme iron. Zinc is needed by enzymes. Calcium is an essential nutrient for bone health the absorption of which peaks around puberty. It is said that after 24 years of age in females and 26 years in males, there is no more calcium accretion. RDA is formulated based on intake required to meet needs of 97–98% population. Various food sources and their RDA are given in **Table 1**.

The Problem

The problem of adolescent nutrition is varied in rural and urban areas. In rural areas, due to large families, uneducated parents, lower income there is decreased intake of fruits, vegetables, meat. Whereas in urban areas, fat and sugar rich food intake along with sedentary lifestyle results in overweight and obesity problems.

This is similar to a study reported in 1998, which found less intake of fruits (28%), vegetables (36%), dairy products among adolescents.[8] Another study in 2014 reported among adolescents fruits, vegetables, dairy, and meat products are less than recommended while fat, oil, and sugar intake were

TABLE 1 **Food sources and uses**

Nutrient	*Food source*	*RDA/day boys*	*RDA/day girls*	*Uses*
Vitamin A	Carrots, spinach, eggs, milk, cheese	900 µg	700 µg	Night vision, affect sexual maturation, prevent infectious diseases
Vitamin B6	Beans, legumes, nuts, wheat bread	1.3 mg	1.2 mg	Heme synthesis, amino acid metabolism
Folic acid	Mint, spinach, pulses, liver	400 µg		DNA, RNA synthesis
Vitamin B12	Milk, milk products, eggs	2.4 µg		Methionine, homocysteine synthesis
Vitamin C	Broccoli, strawberries, citrus fruits, sweet potato, amla	75 mg	65 mg	Collagen synthesis, antioxidant, non-heme iron absorption
Vitamin D	Cheese, butter, fish, fortified milk	600 IU		Calcium metabolism, bone health
Iron	Bengalgram, beetroot, apple			Heme synthesis
Calcium	Ragi, cheese, milk, fish, cauliflower, curry leaves			Bone health
Fiber	Fenugreek, dals,			
Protein	Pulses, ground nut, cashew, almond, meat, egg white, cheese			Muscle mass
Fats	Vegetable oil, ghee, vanaspati			
Carbohydrates	Rice, tapioca			Source of energy

higher. Also adolescent females had better nutritional knowledge but refused eating for fear of weight gain.[9]

Risk Factors for Poor Nutrition

- High fat, high sugar, low nutrient foods like French fries, chips, carbonated drinks are of low cost and available easily
- False belief that healthy foods are not tasty
- Poor knowledge and awareness
- Poor parental modeling
- Disordered eating due to fear of weight gain, building muscle mass

- Social media influence
- Skipping breakfast or having a hurried breakfast

Gender Differences

There is a requirement of about 2,200 calories per day among adolescent girls and 2,500–3,000 calories/day among adolescent males.[10] Like with energy requirement there are differences in requirements between the two genders. Males have more fat free mass and greater skeletal mass. Girls have more fat mass. Prepubertal, both genders have 15% fat content. But after puberty, girls have 20% and boys have 10% fat content in their body.[11] On average girls grow 5–20 cm and boys grow 10–30 cm during adolescence.[5] In view of increased growth spurt, boys require more proteins than girls.

Eating Disorders

These are characterized by wrong food choices with excess concern about body image. It is more common among girls than boys. This unhealthy eating, which involves skipping entire group of nutrients like carbohydrates can lead to physical and psychological illness. The commonly encountered eating disorders are:

- *Anorexia nervosa:* This condition involves eating less than required to maintain lean body image. Although they are undernourished, anorexic adolescents consider themselves overweight and restrict food intake. The gross imbalance in nutrition with depressed estrogen levels manifests as stunted growth, poor bone health, and menstrual abnormalities like primary or secondary amenorrhea.
- *Bulimia:* This category of people tend to binge eat and induce vomiting by self to maintain lean body image. They lack self control and do not restrict their carbohydrate or fat intake. Later concern over body image forces them to purge, use laxatives, slimming pills, and perform strenuous exercise to lose weight. The repeated vomiting can cause dental problems, GI problems.

Poor nourishment can affect physical and mental health of the adolescent, reduce their energy levels, and decrease their immune response. Anemia adolescents tend to have lower memory and perform poor on tests. The score improve with iron supplements.

Complications

Adolescents tend to take 40% of calorie intake from these fat and sugar rich foods such as soda, fruit drinks, pizza, burgers, desserts.[12] These foods can deplete body's nutrition stores and increase excretion of zinc, calcium. Poor nutrition leads to stunted growth, overweight, and obesity problems.

Nutritional deficiency can also manifest as psychological problems such as anxiety and depression. Intake of high sugar diet leads to risk of dental caries, diabetes, obesity in future. They have altered lipid profile and suffer from hypertension, heart disorders, stroke risk as adults. Malnourished adolescent girls tend to have pregnancy complications such as anemia, low birth weight, preterm labor, lactation difficulties. Poor food habits increases the risk of esophageal, stomach, and colorectal cancer.

How Can We Improve It

Though adolescents crave for independence, they still look up to their parents. So it becomes responsibility of a parent to follow healthy eating habits, which in turn the adolescent will follow.

Make the teen involve in grocery shopping and planning the meal. This way they buy food of their choice and in turn will not complain about the food available.

Experiment with recipes: Instead of repeating the same dishes, present the healthy food choices such as pulses, cereals, and vegetables in a more appealing way. Attempt different cuisine and prepare the meal according to the adolescent's taste preferences so that they enjoy having such food items.

Follow regular meal times to avoid excess or unhealthy food intake. Teach children to eat only when they are hungry not out of boredom. This habit cuts down unnecessary food intake.

Ensuring breakfast intake: This improves memory and concentration. Adolescents who have regular breakfast are healthier and have optimal body weight than those who don't. It is better to choose a food rich in fiber, low in fat and sugar for breakfast.

Snacks: Snacking is a common reason of junk food intake. Avoid buying foods you don't want the adolescent to have. Instead keep healthy snacks available such as nutritive cookies, yogurt, nuts, fresh fruits.

Having meals as a family at least once a day. It is not possible to have all meals together but if we eat together once a day, parents will also be aware of the food choices and habits of the adolescent. This can help us in guiding them in the right direction.

In the present scenario of nuclear homes and working parents, ordering food seems easier and affordable for the parents and children. Instead of choosing junk food, if we make healthy food available, either by cooking or from restaurants, adolescents will start considering it.

Eating out: While eating out, it becomes responsibility of parent to make sure healthy choices are made without making the adolescent feel forced. Indulging oneself while eating out is reasonable if it is done occasionally.

Now that we eat out much more than earlier, it is important to watch what we eat.

Liquids: Plenty of water intake is a must to avoid getting dehydrated. Caffeine, although a nervous system stimulant, is harmful in increased amounts and result in sleep disturbances. Restrict to one or two cups of coffee a day or choose healthy alternatives like herbal tea.

Dieting: The social media influence has made all teens body conscious. Teens put themselves through rigorous diets and exercise to avoid body shaming. It is necessary to help the teen follow a healthy diet plan and improve their self confidence. This can be achieved by a parent, teacher, or counselor.

For those concerned of weight, advise to restrict calorie intake by reducing portion size instead of avoiding a particular group of food. Prefer non-processed food to avoid weight gain.

Avoid long hours of TV, games, or computer. Adolescents hooked to their screens don't monitor what they eat and stuff themselves up with junk food and spoil their health. Restrict screen time to 2 hours a day and engage them in physical activity. Making sure our children are not couch potatoes can improve their health and quality of life.

Physical activity: Moderate intensity activity helps in improving bone health, muscle mass, and strength. It also prevents chronic diseases in future. It can be as bursts of activity or organized sports or running, cycling, swimming. Activity maintains blood circulation, oxygen supply, and improves concentration.

USDA has formed a MyPlate with five groups of food—grains, vegetables, fruits, dairy, and protein.[13] It provides information on nutritive values and also suggests food habits for people older than 2 years. The basic suggestions include making fresh fruits and vegetables 50% of food intake, using whole grains, low fat or fat free milk, and varying food choices to keep it interesting.

Adolescents are knowledgeable and exposed to information through schools, and colleges. During this period we can correct deficiencies that occurred in early life and establish good dietary habits by various programs.

National Programs

National Nutrition Policy, 1993, to improve malnutrition through direct interventions among susceptible groups such as adolescent girls.

Kishori Shakti Yojana, 1991—to improve nutrition, health and development of adolescent girls in the age group of 11–14 years. This scheme is slowly phased out and followed with Adolescent Girls scheme, 2010, under ICDS, which covers around 508 districts by 2018. This provides home ration or hot cooked meal for 11–14 year old girls, 600 calories, 18–20 g protein and

required micronutrients per day. Iron and folic acid supplementation, health checkups are also included under this scheme.

National nutritional anemia prophylaxis program, operated under RCH, 100 mg elemental iron and 0.5 mg folic acid for 100 days for adolescents. Weekly Iron and Folic Acid Supplementation (WIFS) launched in January 2019 to provide weekly iron and folic acid tablets, deworming twice a year, and counseling on healthy nutrition for adolescents.

Mid-day meal programme, initially launched by Tamil Nadu in 1961, to provide free meals to school going children to ensure nutrition and school enrollment.

National Policy for Children, 2013, states the right to life, health, nutrition is the right of a child and State should secure access, provision, and promotion of services to ensure child is safeguarded against hunger and malnutrition.

National Food Security Act, 2013, covers 75% of rural and 50% of urban population, which are almost 2/3rd of population to receive subsidized food grains through fair price shop and provide free mid-day meal for children between 8–14 years at schools.

SABLA, Rajiv Gandhi Scheme for Empowerment of Adolescent Girls (RGSEAG), 2011, divides target group of adolescne tgirls into 11–15 years and 15–18 years and provides them nutrition, health, education, self development, and empowerment.

National Nutrition Strategy aims to reduce prevalence of anemia by one third of NFHS 4 levels by 2022. Of 17 sustainable development goals, 12 are relevant for nutrition showing the importance given to proper nutrition.

POSHAN Abhiyan 2018–2020 launched to improve adolescent nutrition with political and program focus. This flagship program focuses on improving nutritional outcome of children, adolescents, pregnant, and lactating mothers through various alliances and strategies.

Food fortification with iron, iodine, vitamin A, and folic acid corrects these deficiencies.

United Nations have launched sustainable development goals; zero hunger is one of those goals. That target is to end all forms of malnutrition by 2030, and address nutritional needs of children under age 5, adolescents, pregnant, lactating mothers, and older persons.

Conclusion

Healthy adolescents are the asset of a nation. It is therefore a collective responsibility of the nation, schools, colleges, and parents to properly nourish and nurture adolescents with adequate vitamins, and minerals to help them grow into healthy adults. Educating and ensuring adolescents take variety of food from each food group along with physical activity will go a long way in bringing up healthy adults.

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Chapter 2

Nutrition in PCOS

Sneha Bhuyar, Ritu Khanna

Introduction

Obesity and Insulin resistance are commonly seen in women with polycystic ovary syndrome (PCOS) and are also interrelated to each other. They also increase the risk for type II diabetes mellitus and heart disease in these women later in life. Managing obesity not only increases insulin sensitivity but also delays onset of diabetes mellitus and improves the reproductive function in them like initiation of spontaneous ovulation. It appears that insulin resistance is at the heart of the etiopathogenicity of both the diseases. Therefore, it is quite logical to aim at reducing insulin resistance as it will result in multiple benefits of improving reproductive function, decreasing risk of diabetes mellitus, and heart disease in the long run.

Lifestyle modifications (physical activity and diet) should be the first line strategy for treatment of PCOS. These are aimed at achieving weight reduction of 5–10% of initial body weight. This loss in body weight ameliorates insulin resistance and simultaneously improves ovulatory function. Suggested interventions for a pragmatic weight loss program are:

- Timing of food intake
- Healthy pattern of eating
- Types of food intake
- Calorie restrictions

Healthy Eating

It is not only that the obese people eat more but in addition, it is their eating pattern and content of their meals that harms their body more by changing their metabolic response to food. Recent studies have proved that eating breakfast early in the day leads to lower intake of total calories throughout the day and along with improves impaired insulin sensitivity. Studies have shown that women taking regular small frequent meals tend to eat less and maintain their body weight in the long run. More than the body weight it is the metabolic response to a meal including insulin sensitivity that prevents women with weight in normal range to not have urge to eat large meals.

Women having irregular breakfasts for a few weeks tend to gain weight. Regular and timely intake of major meals in obese women cannot be overstressed. One should not go more than 4–5 hours between meals. Skipping meals can lead to overeating and swings in blood sugar.

Take healthful meals with at least three food groups and healthful snacks with two food groups. Small sized meals and snacks should be eaten at regular intervals throughout the day. This will not only keep the blood sugar level within a narrow range and prevent significant surges in the insulin response and therefore avoid that feeling of being "over-hungry," which often leads to overeating. Some studies have shown that people who eat small and frequent diets tend to lose weight and maintain it. According to the American Heart Association the meal frequency and timing are the important parameters in the nutrition management of chronic diseases, leading to healthier lifestyle and reduction in cardiometabolic risk factors.

Calorie Requirements and Restrictions

Dietary management plan takes into account calorie requirement of the individual. The recommended calorie requirements of women (lean adult females) are as follows in **Table 1**.

Women with body weight more than normal have large calorie requirement which further increases if they are advised exercise. To achieve the aim of weight reduction, obese women with PCOS are advised to cut down on their calorie intake as the first step. Secondly they are told to have moderate aerobic exercise for half an hour every day. One can easily achieve a weight loss of a kilogram per fortnight if the program is followed in a disciplined manner.

Glycemic Index and PCOS

Glycemic index of foods defines their capacity to raise blood sugar level. Simple carbohydrates are easily digestible and rapidly absorbed and cause a large rise in blood sugar levels causing a large insulin response. On the other hand complex carbohydrates having fiber, vitamins, and minerals take

TABLE 1 **Recommended calorie intake for lean adult females**

Age (years)	*Activity level*		
	Sedentary	*Moderate*	*Active*
19–30	2,000	2,000–2,200	2,400
31–50	1,800	2,000	2,200
> 51	1,600	1,800	2,000–2,200

longer to digest and cause a less immediate impact on blood sugar levels and a small and sustained insulin response. Meals containing food groups having a low-glycemic index tend to improve insulin resistance whereas foods with a high-glycemic index worsen it.

The affect of glycemic index of various food groups have a more important role in maintaining metabolic health rather than the total amount of carbohydrates in the diet.

Eat Fewer Carbohydrates

Blood glucose and insulin are proportionate to each other; the more the glucose in the blood the more insulin is secreted. The main dietary treatment is to eat small amounts of carbohydrates so that less insulin is secreted. In any meal the proportion of carbohydrate should be reduced to about 25% of the plate, and should be less processed, such as whole fruits (includes fiber) instead of fruit juices as this can blunt the surge in insulin secretion.

Eat More Plant Foods

Eating more of whole grain breads and whole wheat pasta and cereals like brown rice and fruits and vegetables, increases dietary fiber intake and helps one feel full on fewer calories. Fiber in these foods being indigestible, slows down the digestion process, and subsequently the release of glucose into the blood, blunting the insulin response. High-fiber diets also help in weight reduction.

Pair Carbs with Protein

Unprocessed carbohydrates (low glycemic index) with lean protein and a little fat (whole-grain crackers with reduced fat cheese) take long time to digest and help increase satiety. They also hold blood sugar steady and help avoid glucose dips that can trigger cravings for carbohydrate rich foods (high glycemic index).

Fats and PCOS

Fats should form 25% of a diet taken by these women. Unsaturated fats are more healthy than the saturated fats. Women with PCOS eating diets rich in omega-3 unsaturated fatty acids with a double bond tend to be at a lower risk of developing metabolic disorders later in life.[1]

Vitamin D Deficiency

Studies have revealed that vitamin D plays a role in various metabolic pathways, including insulin metabolism, and affects the pathogenesis

of insulin resistance and PCOS.[2-4] The mechanism behind this effect is still unknown, but a possible role for ovarian dysfunction in the mechanisms that regulate apoptosis has been reported.[5] Moreover, due to its immunomodulatory role, lack of vitamin D may cause inflammatory responses leading to insulin resistance.[6]

Conclusion

Obesity, as such appears to be a disorder of caloric imbalance that results from intake of calories more than that can be consumed by the body. It cannot occur without intake of excess food. Lifestyle change in the form of small diets taken at regular frequent intervals and moderate exercise, half an hour every day, has proven to be a good initial strategy, in breaking the vicious cycle of increased body weight and metabolic milieu of insulin resistance in obese women having PCOS. It has been observed that a meagre 5% reduction of their body weight improves insulin sensitivity and restores ovulatory function in majority of such women. These women are recommended to take a balanced diet with just enough carbohydrates especially rich in fiber from whole grains, legumes, vegetables, and fruits having low glycemic index.

This strategy not only helps in improving short-term reproductive goals, but also in addition, if practised lifelong, it reduces in them the risk of developing type II diabetes mellitus and cardiovascular disease, which otherwise they would have been more prone to, later in life.

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Chapter 3

Preconceptional Nutrition

Reena Wani, Rashmi Jalvee

Introduction

Pregnancy is an exceptional phase in a women's life; in that her health, well-being, and diet influence the health of not just one but two individuals. There is now a growing recognition of the importance of adolescent and women's preconception nutritional status to improve maternal and infant outcomes. A World Health Organization (WHO) report shows that preconception care has a positive impact on maternal and child health outcomes.[1]

The three-months preceding pregnancy constitutes the preconception period. This period is now being redefined according to:[2]

- *Biological perspective:* Period before embryogenesis (weeks before pregnancy)
- *Individual perspective:* A conscious intent to conceive (weeks to months prior to pregnancy)
- *Public health perspective:* Period to address risk factors, viz., obesity, diet, etc. (months to years)

Preconception care aims to provide biomedical, behavioral, and social health interventions to women and couples before pregnancy occurs. It involves providing care to improve the health of women and addresses behaviors and risk factors that may lead to adverse maternal and fetal outcomes.

An important aspect of preconception care is the women's nutrition. Maternal nutritional deficiencies can be rectified by micronutrient supplements during pregnancy, but they are sometimes not enough to improve long-term pregnancy and fetal outcomes. Several factors involved in determining the woman's nutritional health include genetic make-up, lifestyle, medical disorders, or drug exposure.

Preconception care addressing nutrition should include dietary adequacy, healthy weight, and any medical nutrition therapy.

Dietary Adequacy

Women in the preconception period should be advised to eat nutrient-rich food. Factors that affect food intake include availability of food, income, woman's beliefs and choices, traditions, cultures, and social, educational, and geographical aspects.

Dietary Supplements

Although many of the requisite vitamins, minerals, essential fatty acids, and other constituents are found in food, the physiologic demands of the woman during preconception and pregnancy may require additional dietary supplementation. Requirements for folic acid, calcium, iron, zinc, vitamin D, vitamin C, and vitamin B increase substantially during pregnancy.

Folic Acid

Folic acid is a B-complex, water soluble vitamin required for DNA synthesis and cell division. Dietary sources include green leafy vegetables, legumes, citrus fruits, cereals, and breads containing folic enriched flour.

The synthetic form of folate is folic acid. Folic acid is used in fortified cereals and supplements to prevent development of neural tube defects (NTDs).

As per the WHO recommendations, women trying to conceive should take folic acid supplement from the time they plan a pregnancy till 12 weeks of gestation.[3]

A Cochrane review concluded that folic acid supplementation taken in the periconceptional period reduced the risk of developing NTDs by 72% and the risk of recurrence of NTDs by 68%, compared with no intervention, placebo, or micronutrient intake without folic acid.[4]

The American College of Obstetrics and Gynecologists (ACOG)[5] recommends supplementation with 400 mcg of folic acid per day for average risk women. Women at increased risk of NTDs, viz., women with a previous pregnancy with NTD, obese women, diabetic with poor glycemic control or with seizure disorders, should be counseled to take 4 mg of folic acid daily.

Iron

Worldwide, the commonest cause of anemia in pregnancy is iron deficiency anemia.[6]

Women of reproductive age are at risk of iron deficiency due to poor diet, menstrual blood loss, and multiple frequent childbirths. Fetal complications include prematurity and intrauterine growth restriction.

Women planning a pregnancy should consume iron-rich foods (meat, poultry, green leafy vegetables, jaggery, and iron-fortified cereals). To reduce

the incidence of anemia in women of reproductive age, WHO recommends intermittent iron and folic acid (IFA) supplementation for menstruating women in areas where anemia prevalence is over 20%.[7]

ACOG recommends that at a preconception visit, screening should be conducted for women with risk factors for iron deficiency for the purposes of identifying and treating anemia.[8]

Vitamin D

Vitamin D is a lipid-soluble vitamin that regulates calcium and phosphate equilibrium, and thus bone metabolism. Vitamin D is produced by the body during exposure to sunlight, but is also found in oily fish, eggs, and fortified-food products. Dietary sources include fortified foods, viz., milk, orange juice, and breakfast cereals. Vitamin D deficiency during pregnancy is known to be associated with pre-eclampsia, low birth weight, impaired glucose tolerance in pregnancy, and impaired growth and bone development in the fetus.[9]

The ideal dose of vitamin D during periconceptional period is unknown. Vitamin D deficient women should be given information on vitamin D sources in the diet and supplementation. The RCOG recommends daily dose of 10 mcg (400 IU) of vitamin D for all during preconception period and pregnancy. Women at high risk of vitamin D deficiency, viz., women with increased skin pigmentation, reduced exposure to sunlight, or obese women are advised to take at least 1,000 units a day.[9]

Calcium

Calcium plays an essential role in the development and maintenance of bone health. During pregnancy, fetus receives its nutrition from maternal sources. When completing a diet history during preconception counseling, it is important to ask about calcium consumption in the food (milk, cheese, sea-food, fortified orange juice, etc.), calcium supplementation, and use of antacids to assess the woman's overall calcium intake. If dietary sources are inadequate, oral supplementation with calcium (1,000 mg) and vitamin D is recommended.[10]

Vitamin A

Vitamin A is a fat-soluble vitamin, not synthesized in the body; available as:

- *Preformed Vitamin A:* Present in foods of animal origin (liver, whole milk). It is absorbed as retinol and converted into retinal and retinoic acid in the body.
- *Provitamin A carotenoid:* Vitamin A present in vegetables and fruits and converted into retinol in the body.

Isotretinoin: A synthetic form (13-cis retinoic acid) of vitamin A used to treat severe, cystic acne.

Vitamin A is required for ocular function, integrity of epithelial tissue, immunity, development of bone, and normal embryonic development.[11]

As Vitamin A is lipid soluble, it crosses the placenta. Although normal fetal development requires vitamin A, high dose of preformed vitamin A supplementation is associated with miscarriage and birth defects that affect the CNS, craniofacial, cardiovascular, and thymus development.[12]

Women planning to conceive and pregnant women should be counseled that vitamin A supplementation above 700 mcg might be teratogenic and should be avoided.[13]

In areas of vitamin A deficiency, WHO recommends a maximum safe dose of up to 10,000 IU daily or 25,000 IU weekly after the first 60 days of gestation.[14]

Dietary sources of vitamin A and beta-carotene should be included in a healthy diet as they do not pose a risk of excessive intake. Vitamin A from beta-carotene is not known to increase the risk of birth defects.

Isotretinoin is known to cause serious birth defects and should not be taken during pregnancy and preconception period. The current recommendation is to discontinue Isotretinoin at least 1 month prior to attempting pregnancy.[15]

Iodine

Iodine is an essential nutrient acquired through the diet. It is essential for thyroid hormones synthesis, which are responsible for regulating growth, development, and metabolism. Iodine deficiency during pregnancy impairs the normal development of fetal CNS, particularly myelination.

Salt iodization is the recommended, preferred strategy to control and eliminate iodine deficiency. WHO recommends a daily iodine intake of 150 g for adults (over 12 years of age) and 200 g for pregnant and lactating women.[16]

Essential Fatty Acids

All women planning a pregnancy should be advised to consume foods rich in essential fatty acids (omega 3 and omega 6 fatty acids). Recent research has addressed the role of omega 3 fatty acids [docosahexanoic acid (DHA) and ecosapentanoic acid (EPA)] in the fetal cognitive and neurological development. These are essential fatty acids derived from sea food primarily from fatty fish. Fatty fish is a known source of contaminants, viz., mercury and persistent organic pollutants, particularly in larger fish species. ACOG recommends that women planning a pregnancy can eat up to 2–3 servings a week (8–12 ounces in total) of a variety of fish in order to avoid the harmful effects of mercury.[17]

Caffeine Intake

In the periconceptional period, women should be counseled that increased caffeine intake (>300 mg/day) may be associated with spontaneous abortions, low birth weight, and other adverse pregnancy outcomes. They should be advised that lowering daily caffeine intake to less than 200 mg/day appears to be safe and does not to be a major contributing factor in adverse pregnancy outcome.[18,19]

Alcohol Intake

Women planning a pregnancy should be informed that consumption of alcohol in the periconceptional period is associated with spontaneous abortion, neural tube defects, and GI malformations, and also correlates with maternal depression.

As per the ACOG recommendations[20]

- Screen women in the reproductive age group for alcohol use.
- Inform them about the potential risks of alcohol consumption.
- Advise women that the effects of consuming alcohol on pregnancy begin early from the first trimester, and that no safe level of consumption has been established.
- Women who are pregnant, planning to become pregnant, or at risk of becoming pregnant must abstain from alcohol use.

The recommendation for nutrient intake is summarised in **Table 1**.

Preconception Weight and Body Mass Index (BMI)

Before embarking on a pregnancy, all women should be counseled to try to attain a body mass index (BMI) in the normal range, because abnormal high or low BMI is associated with infertility and adverse maternal and fetal outcoms.

Obesity, defined as a BMI of 30 kg/m^2 or greater, is associated with:

- *Maternal risks:* Type 2 diabetes, hypertension, infertility, thromboembolic disease, cesarean delivery.
- *Perinatal risks:* Preterm delivery, stillbirth, macrosomia, low Apgar scores.

The risks associated with high BMI are best addressed before conception because during pregnancy, weight loss is not recommended.

All women with a low BMI should be assessed for eating disorders and distortions of body image.

Interventions to improve weight should support a healthy lifestyle:

- addressing individual knowledge and skills,
- reducing exposure to foods low in nutritional value and high in calories, and
- increasing opportunities for physical activity.

TABLE 1 **Peri-conception nutrition supplementation**[21]

Nutrient	*Target population*	*Recommended dose*	*Evidence*
Folic acid	All women planning a pregnancy Women at high risk of NTDs (GDM, previous NTD, obesity, anticonvulsant medication)	400 mcg daily from 4 weeks preconception to 12 weeks of gestation 4 mg daily from 4 weeks preconception to 12 weeks of gestation	Prevention of NTD such as spina bifida and anencephaly
Iodine	All women	150 mcg daily while pregnant and breastfeeding	Production of maternal thyroid hormone, fetal brain, and CNS development
Iron	Women with iron deficiency on blood tests	Daily oral iron tablets containing at least 60 mg of elemental iron	Prevention of anemia
Vitamin D	Women with vitamin D deficiency on blood tests	1,000 IU/day (vitamin D 30–49 nmol/L) 2,000 IU/day (vitamin D <30 nmol/L)	Essential for bone development in the fetus
Calcium	Women with inadequate dietary intake	At least 1,000 mg daily	Essential for fetal skeletal development Prevention of pre-ecalmpsia
Vitamin A	All women	• No risk with dietary sources • Vitamin A supplements up to 700 mcg/day • Synthetic derivatives of Vitamin A should be stopped at least 1 month prior to pregnancy	Increased risk of miscarriage and CNS malformations
Caffeine	All women	Limit to 300 mg or less per day (equivalent to two to three standard cups of coffee)	Increased risk of fetal growth restriction

Nutrition and Existing Health Conditions:

- The role of nutrition in chronic illnesses such as hypertension or diabetes must be addressed.
- Chronic conditions such as diabetes, hypertension, polycystic ovarian syndrome (PCOS), and metabolic syndrome often require medical nutrition therapy as part of their preconception care.
- Acute conditions such as anemia are treated with diet and medication.
- Other conditions, like epilepsy and HIV infection, require medications that may alter nutritional status.
- Some high-risk pregnancy conditions like preterm birth, gestational diabetes, or hypertension may reoccur in subsequent pregnancies.
- Several of these adverse health conditions have a nutrition component, which should be addressed between subsequent pregnancies.

Conclusion

Healthy diet is essential for optimal pregnancy and fetal outcome. Information on a healthy, well-balanced diet that includes vegetables and fruits should be given to all women especially those embarking on a pregnancy. As a component of preconception care, issues regarding nutritious diet, weight gain, and dietary supplements should be addressed.

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Chapter 4

Maternal Nutrition: A Way Forward

T Ramani Devi, T Mathangi

Introduction

Birth outcomes and long-term effects of the health of the offspring are affected by maternal nutrition, which is a modifiable risk factor. "An undernourished mother gives birth to an undernourished baby, which becomes a vicious cycle of undernutrition" according to UNICEF. Nutrition during the first 1,000 days of child's life gives a critical window of opportunity, when managed properly can bring about a healthy child.

Fetal growth and development are promoted by the amount of micronutrients and the macronutrients the mother consumes. Adverse pregnancy outcomes occur secondary to maternal under nutrition or over nutrition.

Even the fetal over nutrition can lead to abnormal fetal programming that can increase diseases occurring childhood, and can extend to adulthood also. Hence, there is a need to monitor, evaluate and alter the diet pattern among women who plan for pregnancy during periconceptional period.

Nutritional Status Assessment

It is prudent to assess the woman's nutritional status in the pre-pregnancy period and this can be best done with a multidisciplinary team including obstetricians, health-care professionals trained in nutrition, family physician, and a registered dietician.

Calorie

Between 350–450 extra kcal/day is needed for a singleton pregnant woman during late trimesters. First trimester does not need extra energy intake.

The energy requirement during pregnancy are as follows:

- Heavy worker: (2925 + 300) kcal/day
- Moderate worker: (2225 + 300) kcal/day
- Sedentary worker: (1875 + 300) kcal/day extra calories

- 1st trimester – 85 kcal
- 2nd trimester – 285 kcal
- 3rd trimester – 475 kcal[1]

We need extra energy for adolescent pregnancies, multiple pregnancies, mothers who have extremely hard physical labor, maternal infection, and malabsorption. Women with chronic energy deficiency land up with maternal and neonatal morbidity and mortality.

Carbohydrate

Dietary carbohydrate is broken-down to form glucose. The RDA for carbohydrate during pregnancy is 175 g/day. Carbohydrate/protein ratio should be adequate to avoid decrease in gestational weight gain. Pregnant women should consume many servings of whole grains, vegetables, and fruits. Processed carbohydrates which have high-glycemic index should be reduced to prevent excess weight gain. Nutrition of the women during pregnancy should include 2–3 bowls of fruits, 3–3.5 bowls of vegetables, food grains, proteins ranging between 6–8 oz and 3 cups of dairy products.

Protein

Around 1 kg of protein is utilized by fetoplacental unit during second and third trimester. The national academy of medicine suggests a protein intake of 1.1 gm/day should be higher than the non-pregnant women. Commercially available high protein powders and drinks should be avoided.

Additional requirement:

- 1 gm/day 1st trimester
- 8 gm/day in 2nd trimester – RDA 1.1 gm/kg/day
- 2 6 gm/day in 3rd trimester- RDA 1.2 gm/kg/day

Fat

The mother must include enough fat in her diet to meet the needs of her growing baby. The recommendation is to include 20–35% of total calories with additional of 8–14 gm/day during 2nd trimester and 11–18 gm/day during 3rd trimester. There is no definite data's regarding the type and quantity of fat intake.

Fiber

Pregnant women need 28 g/day of fiber, which modulates gut micro-biotome. It reduces respiratory problems like asthma for the newborn and the GP visits for common cold and cough.

Micronutrients

Extra vitamins and minerals that are not available through diet should be supplemented. This includes, 30 mg of iron, elemental calcium of 1,000 mg/day, 40 mcg/day of folic acid (in women with previous H/O neural tube defect more amount is required), 150 mcg of iodine, vitamin D up to 1,000 IU are required. Other vitamins like A, B, C, E, and Zinc are needed in adequate amounts.[2,4]

Folic Acid

Neural tube defects can be avoided by periconceptional supplementation of folic acid up to 40–80%. Folic acid can help to prevent birth defects like NTD, congenital heart disease, cleft lip, and palate.

The dietary sources are leafy green vegetables, yeast extract, and citrus fruits such as oranges (RDA: 600 mcg/day).

Supplementation: 0.4 mg/day during preconception and early pregnancy.[3]

In women who are at risk of babies with neural tube defects, higher dose of 4–5 mg is needed per day.

Vitamin B

- 770 mcg/day is the RDA required for the antenatal mothers
- B1: RDA for pregnant women is +0.2 mg/day
- B2: RDA for pregnant women is +0.2 mg/day
- B3: RDA for pregnant women is 2 mg/day
- B6: RDA for pregnant women is 2.5 mg/day

Vitamin B12

Vitamin B12 is a water-soluble vitamin and also called as cobalamin. It synthesized by only microorganisms in the gut. It is needed to absorb iron, calcium and vitamin A. Vitamin B12 is needed for myelinogenesis, brain, and fetal growth.

DNA synthesis, fatty acid, and amino acid metabolism of every cell depend upon vitamin B12 levels. It is obtained from animal sources, plant sources, and fortified food sources.

B12 concentrations of less than 148 pmol/L led to LBW babies and preterm birth according to 18 studies which included 11,216 patients.

Similar to folate deficiency, B12 deficiency is found to be associated with neural tube defects.

Its deficiency leads to megaloblastic anemia, increased risk for adverse pregnancy outcomes for both mother and fetus. These risks include neural

tube defects, early miscarriage, pre-eclampsia and IUGR. The neurological and developmental delays are irreversible.

Iron

There is a global prevalence of anemia beyond 50% in women of reproductive age group. Prevalence of anemia in India among pregnant women is around 40%. Hence, women need micronutrients like iron and folic acid to correct anemia.

Iron deficiency causes maternal anemia, premature labor and FGR babies. Doubling the consumption of iron to approximately 30 mg/day prevents iron deficiency anemia.

Oral intake of iron on alternate days is better tolerated and corrects anemia. Pregnant women should receive oral iron supplementation when the hemoglobin (Hb) < 11 g/dL during the first and last trimester and ≤10.4 g/dL during the second trimester and serum ferritin <40 ng/mL. One option is 65 mg of elemental iron (325 mg ferrous sulfate) every other day is well tolerated. Higher doses of iron supplementation reduce the iron absorption. Iron and vitamin B12 deficiency are common who take in vegetarian diet.

Calcium and Vitamin D

Pregnant women need 500 mg of extra calcium than non-pregnant women. Vitamin D > 4,000 IU/day may lead to toxicity. Though the exact dose is not defined.

Vitamin D is essential for maternal calcium homeostasis and fetal bone development. Deficiency of vitamin D leads to IUGR, pre-eclampsia, increased risk of LSCS, PTB, abnormal GTT, rickets, osteopenia, and neonatal hypocalcemia. In later life it may lead to asthma, multiple sclerosis, neurological disorders, autoimmune disorders, and cardiac failure. Its natural sources are sunlight, Cod liver oil, fish, egg, butter, and cheese.

As per RDA, pregnant and lactating women need 1,000 mg/day of elemental calcium.

IOM in 2010 suggests 600 IU/day vitamin D3 in all women of reproductive-age group, antenatal and lactating mothers and up to 2,000 U/day in high-risk group. Commercially available non-prescription products contain only vitamin D2 rather than vitamin D3 which is the active form.[5]

Role of DHA

Docosahexaenoic acid (DHA) is essential for the neuronal development of the baby and prevents preterm birth and pre-eclampsia. DHA is found in ocean fish, oily fish, Mackerel, Salmon, Herring, and Sardine, which should be taken twice weekly. Tuna and Sword fish consumption should be limited

due to their methyl mercury content. Pregnant and lactating mother are not advised to consume raw fish. Non fish eaters should be supplemented with 300 mg of omega-3 DHA.

Essential Fatty Acids (EFA)

The EFAs (omega-6 and omega-3) are necessary for optimal formation of the brain and eyes.

RDA: Omega-6–13 g/day and omega-3–1.4 g/day

Omega-3 fatty acids help in cognitive development and prevents allergy. Antenatal mothers should avoid raw animal-based food, raw eggs, unpasteurized milk, and packaged foods. Washing of raw fruits and vegetables are advised to avoid food borne infections like Toxoplasmosis and Listeriosis, which result in preterm birth, stillbirth, and fetal damage.

Women who are on Vegan diet should be advised supplementation of iron, DHA, zinc, and vitamin B12 as needed. If not, there is increased risk of LBW babies, pre-eclampsia, and inadequate brain development.

Well balanced Ovo-lacto vegetarian diet with vitamin D, folic acid, iodine, vitamin B12, iron, and zinc are better. Animal protein quality is better than vegan.

In general, pregnant women should have adequate exercise, avoid smoking, alcohol, and intake of excess caffeine.

Vitamin A

Current evidence does not support vitamin A supplementation for better outcome of pregnancy, rather teratogenicity can happen because of excess intake.[3]

Choline

Dietary intake alone is sufficient and there is no need for supplementation.

Natural animal proteins like eggs, meats, fish, and dairy and plant-based sources like navy beans, Brussels sprouts, broccoli, and spinach are enough to meet the daily needs.

Zinc

Daily food intake can supply the RDA of zinc ranging between 9–22 mg/day.

Iodine

As per WHO recommendation, pregnant and lactating woman should take 250 mcg of iodine. ATA recommends 150 mcg of iodine in the form of potassium iodide to be supplemented daily. Cochrane has inadequate data's

regarding the benefits and harms of routine iodine supplementation. Extra supplementation of iodine can lead to fetal goiter.

Vitamin E

There is no benefit of vitamin E supplementation in preventing stillbirth, PTB, pre-eclampsia and LBW.

Vitamin C

Vitamin C supplementation has got no effects according to Cochrane review.

Gluten-Free Diet

Gluten-free diet does not have any significant health benefits.

Low Carbohydrate Diet

The restricted carbohydrate intake along with reduce folic acid intake increases the risk of having an infant with a neural tube defect. Between 0.4–0.8 mg folic acid has to supplemented periconceptionally. (NTD; odds ratio 1.30, 95% CI 1.02–1.67—review data from National Birth Defects Prevention Study.)

Lactose Intolerance

Usually, pregnant women have improved lactose intolerance probably because of slower intestinal transit. Severe cases can have calcium supplementation or calcium fortified foods

Artificial Sweeteners

It is safe to take if less than the acceptable daily intake (ADI) and very rare to exceed ADI. ADI for aspartame is 50 mg/kg/day and 1 diet coke has 131 mg aspartame per 355 mL can. ADI for stevia is 5 mg/kg/day.

AAP and FDA have concluded saying aspartame is safe during pregnancy and lactation. There are no RCTs yet to prove the same.

Sugar Containing Beverages

Ideal to avoid frequent intake. They are called "Empty calories" as they do not add any nutritional value.

Fasting

During the month of Ramadan, pregnant women also fast during the day and it is not found to have any impact over the uterine blood flow as well as the fetal growth in a previously healthy woman.

Caffeine

A 2017 systematic review concluded that consumption of up to 300 mg caffeine/day in healthy pregnant women is generally not associated with adverse reproductive and developmental effects. 1 cup of filter coffee has average of 95 mg of caffeine.

Herbal Products

The most common products suggested were Herbal teas, Chamomile, Ginger, Cranberry, Raspberry leaf, Echinacea, and Ephedra. No RCT but studies have not recommended any of the herbal products except ginger.

Liver-based Foods

It is generally a practice in India to advice excess liver-based foods because of the natural source of iron but we also have to note that liver patties/sausages have excessive vitamin A content, and hence it is prudent to limit the intake.

Conclusion

Pregnant women should be advised to take proper balanced diet with proper proportion of carbohydrates preferably whole grains, proteins, fats, vegetables, and fruits. They should reduce empty calories and take food with high nutritive value with appropriate calories. No additional calorie is needed during 1st trimester and moderate increase in calories (340–450 kcal/day) during 2nd and 3rd trimester. Extra needs should be based upon the pre-pregnancy BMI, nature of work, and this must be assessed, calculated, and discussed with every patient.

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Chapter 5

BMI—What We Need to Know?

Alpana Agrawal, Indranil Dutta

Introduction

Body mass index is one of the most popular determinants of health. It is also known as Quetelet II index as it was coined by Adolf Quetelet of Belgium in 1832. The Quetelet index was termed the Body Mass Index (BMI) in 1972 by Ancel Keys.[1,2]

BMI identifies individuals whose weight is disproportionate to their height. This tool is used in different fields of science, in laboratories, in medical offices, in homes, and gyms by professionals, scientists, researchers, and trainers, just about everywhere and everyone.[3]

BMI is inexpensive, noninvasive, and a simple method to measure body fat. It helps to estimate the risk of underweight and overweight/obesity of a person. Today, due to rising standards of living and a sedentary lifestyle, weight gain and obesity are posing a health risk all over the world. Obesity is considered a chronic disease, affects populations of all age groups in developed as well as developing countries.[4] The phenomenon of underweight and obesity has given rise to the coining of a new set of diseases known as civilization diseases, e.g., polycystic ovary syndrome (PCOS), infertility, hypertension, stroke, DM, atherosclerosis, certain cancers, and nutrition disorders.[3]

It has been found that with an increase in body fat and BMI levels there is a proportionate rise in future health risks, morbidity, and mortality. Epidemiological data shows that for BMI between 25–30 kg/m^2 there is a modest increase in mortality. With a BMI of ≥30 kg/m^2, mortality rates are 50–100% more, especially due to cardiovascular diseases, than with a BMI of 20–25 kg/m^2.[5,6]

Since BMI measurement is dependent on weight and height so with the availability of proper equipment, it can be accurately measured and calculated.[7] Therefore, BMI is considered a reasonable measure to screen for obesity and its resultant health risks.

BMI has its limitations too. Even though it is used as an index of a person's fatness, but since it does not measure adipose tissue so it does not diagnose the fatness of the body. It is a measure of excess weight rather than excess

body fat.[2] BMI doesn't distinguish between fat, muscle, and bone mass, so a person who has a remarkable lean body mass and very little body fat can be placed in an overweight category. Moreover, BMI does not give information on the mass of fat in different body sites, whereas it has been found that the physical distribution of fatty tissue significantly affects mortality and morbidity.

To determine the health risk of an individual, age, sex, ethnicity, evaluation of diet, physical activity, and family history must be taken into account.[8,9]

Definition

BMI is a person's weight in kilograms divided by the square of height in meters. It is an inexpensive and easy screening method for defining the weight of an individual—underweight, healthy, overweight, and obese.

Calculating BMI

- Metric measurement system:
  BMI = Weight in Kilograms/(Height in Meters) × (Height in Meters)
- For the Imperial system of measurement:
  BMI = (Weight in Pounds/[(Height in inches) × (Height in inches)] × 703

WHO Classification

The classification of adults according to BMI, as recommended by WHO, is depicted in **Table 1**. The table also shows relationship between BMI and risk of comorbidities though it is affected by factors such as diet, level of physical activity, and ethnic group.

Alternative Methods to Assess Body Fatness

Other methods to measure body fatness are skinfold thickness measurements (with calipers), underwater weighing, bioelectrical impedance, dual-energy X-ray absorptiometry (DXA), and isotope dilution[10] Another simple measure of fat distribution is the waist circumference. Although the body fatness and the risk of obesity-related health problems of an individual are better indicated by these measures, they are not very popular as they are expensive, invasive, not available easily and widely, require highly trained personnel/complex technologies, or are difficult to standardize.[2,7]

Interpretation of BMI for Children and Adolescents

The formula used to calculate BMI in children and adolescents is the same but it is interpreted differently. BMI of children and adolescents needs to be age- and sex-specific because, with age, the amount of body fat undergoes

TABLE 1 **WHO classification of adults according to BMI**

Weight status	*Body mass index (BMI) (kg/m²)*	*Risk of comorbidities*
Underweight	<18.50	Low (but risk of other clinical problems increased)
Normal range	18.50–24.99	Average
Overweight	≥25.0	
Preobese	25.00–29.99	Increased
Obese class I	30.00–34.99	Moderate
Obese class II	35.00–39.99	Severe
Obese class III	≥40	Very Severe

TABLE 2 **BMI-for-age categories and corresponding percentiles**

Percentile ranking	*Weight status*
Less than 5th percentile	Underweight
5th percentile to less than 85th percentile	Healthy weight
85th percentile to less than 95th percentile	Overweight
Equal to or greater than the 95th percentile	Obese

changes and the amount of body fat is different between girls and boys. These differences are taken into account in the CDC BMI-for-age growth charts which show BMI as a percentile ranking as depicted in **Table 2**. BMI at or above the 95th percentile of children of the same age and sex is considered to define obesity among 2- to 19-year-olds.[11]

Factors Affecting BMI[12]

Genetic Factor

- Many studies have identified a specific defect in genes that synthesize the hormone leptin, a natural appetite-suppressant hormone. It is produced by fat and acts on the hypothalamus to regulate body weight.
- Congenital absence of leptin produces continual hunger and marked obesity in children. The second genetic defect observed is the body's response to the signal provided by leptin, which determines how much one eats, how much energy one spends, and ultimately one's body weight.

Psychological Factor

- Studies have shown that obese people are about 25% more likely to experience a mood disorder like depression compared with those who are not obese.

- Many obese people eat in response to negative emotions such as boredom, sadness, or anger as eating soothe fears, sadness, and worry.

Lifestyle Factor

- *Level of physical activity:* Sedentary lifestyle can lead to obesity.
- *Dietary habits:* A large consumption of foods high in sugar and fat increases the likelihood of weight gain.
- *Sleeping hours:* Insomnia or lack of sleep can cause hormonal imbalance that increases appetite or craving for foods high in calories and carbohydrates.

Economical Factor

- Economic constraints contribute to unhealthy food choices.
- Among low socioeconomic groups, they tend to buy the product which is cheaper to reduce their food budgets while maintaining diets similar to the average population diet.
- And so the proportion of energy by meat, dairy products, vegetables, and fruits decreases, but the proportion by sweets, added fats, and cereals increases that can lead to obesity.

Clinical Importance of BMI

Elevated BMI is extremely clinically relevant. It increases the risk of developing a range of medical complications linked with excess weight.[7,8,12,13]

- Idiopathic intracranial hypertension
- Stroke
- Cataract
- Coronary heart disease
- Diabetes
- Dyslipidemia (high LDL & triglycerides, low HDL)
- Hypertension
- Pulmonary disease—Abnormal function, Obstructive sleep apnea, Hyperventilation syndrome
- Nonalcoholic fatty liver disease—Steatosis, Steatohepatitis, Cirrhosis
- Gall bladder disease
- Severe pancreatitis
- Gynecologic abnormalities—Abnormal menses, Infertility, PCOS, etc.
- Osteoarthritis
- Phlebitis venous stasis
- Chronic inflammation and increased oxidative stress
- Carcinomas—Breast, Endometrial, Cervix, Colon, Esophagus, Pancreas, Kidney, Prostrate, Gall bladder, and Liver

- Gout
- Clinical depression, Anxiety, and other mental conditions

Metabolic Disorders

- Significant correlation between ↑ BMI and Insulin Resistance.
- ↑ BMI indicates more adipose tissue. With 10 kg of excess weight, there is 10–30% increase in beta-cell mass leading to increased insulin secretion. This in turn results in down-regulation of tissue insulin receptors, leading to insulin resistance, predisposition to diabetes.[14]
- People with BMI 35.0 kg/m^2 have a sixfold increased risk of developing diabetes.

Cardiovascular Diseases

- The high-risk factors for coronary heart disease, i.e., hypertension, dyslipidemia, and diabetes are all associated with raised BMI.[15]
- Obese women have a 30% higher risk of mortality due to cardiovascular diseases.

Respiratory System

Increased BMI is associated with the obesity hypoventilation system. It can cause breathing problems like obstructive sleep apnea, which is known to be correlated with pulmonary hypertension, abnormal heart rhythms, and results in excessive fatigue.[4]

Gastrointestinal System

Raised BMI is associated with gastroesophageal reflux disease, cholecystic disease, colon carcinoma, and hepatic disease. There is regurgitation of gastric contents into the esophagus because increased abdominal pressure due to obesity pushes against the cardiac sphincter in the stomach, thus resulting in GERD.[16]

Liver

Deposition of fat within the liver (non-alcoholic steatohepatitis) results in inflammation, injury, and scarring. This scarring is as detrimental as alcoholic cirrhosis.[16]

Integumentary System

Increased adipose tissue causes inflammatory changes in the dermis, which results in immune-mediated hidradenitis suppurativa and also psoriasis. A low BMI is associated with fine hair growth known as lanugo and dry, thickened dermis with less exfoliation.[17]

Reproductive System

- There is a higher incidence of irregular menstrual cycles, anovulation, subfertility, and infertility in women with a BMI of 30 kg/m^2
- Obesity is strongly associated with PCOS
- It impacts pregnancy outcomes (RCOG)
- Associated with poor prognosis with assisted reproduction. BMI 35 kg/m^2 decreases pregnancy rates by 50%
- There is an increased risk of abortion, stillbirth, preterm, pre-eclampsia, fetal macrosomia, GDM, VTE, PPH, operative delivery, anesthetic complications, post-op wound infection, and increased perinatal mortality.

Genitourinary System

A low BMI can cause acute kidney injury due to excessive restriction of food/fluid, purging, and use of laxatives, which can result in dehydration and pre-renal injury. The associated electrolyte abnormalities can lead to nephrolithiasis, and post-renal injury. Hypokalemia and hypovolemia can cause chronic kidney disease.[18]

Carcinoma

Progenitor cells are needed for a favorable tumor environment and they are mobilized by white adipose tissue, so raised BMI is found to be associated with an increased level of circulating progenitor cells. Some studies have shown an association between high BMI and cancers of breast, prostate, endometrium, ovary, and colorectal carcinoma.[4,19]

Neuronal Tissue

High BMI indicates more adipose tissue. The hormone leptin is produced by adipocytes, which allow energy expenditure by the body and also have a strong association with memory formation (it may have a correlation with learning disabilities in underweight children).[20]

Psychosocial Health

- Poor body image
- Social stigmatization/discrimination (it reduces a person's confidence, impairs one's ability to perform optimally, hence leading to under-achievement)
- Lower education levels
- Difficulty in marriage
- Stigma of infertility

Limitations

- As with most measures of health, BMI is not a perfect test, it is a measure of excess weight rather than excess body fat. [7]
- It is only an estimate and it doesn't take into account
  - gender
  - age
  - ethnicity
  - body composition
  - comorbidities
  - It ignores waist size, which is a clear indicator of obesity level
- It makes no allowance for the relative proportions of bone, muscle, and fat in the body. But bone is denser than muscle and twice as dense as fat, so a person with strong bones, good muscle tone, and low fat will have a high BMI. Thus, an athlete with a high-lean body mass (muscle and bone) and fit, health-conscious persons who work out a lot may be classified as overweight or even obese.
- At the same BMI, females have more body fat than males. Asians have more body fat than whites.
- It may underestimate body fat in older persons and others who have lost muscle.
- BMI calculation shouldn't be used for pregnant women, children, or the elderly.

Related Testing

- Tests to be done for individuals with BMI 30—Lipid profile, Thyroid profile, diabetes screening.
- Tests to be done for individuals with BMI 18—Thyroid profile, comprehensive metabolic panel, psychiatric screening, malabsorption (standards of care in the American Diabetes Association Diabetes Care annual update).
- A cancer workup should be done for rapid and unintentional weight loss.

Management of Overweight and Obesity[12]

- *Behavioral Strategies:* Self-monitoring, Social support, Stress management, etc.
- *Dietary Intake:* Reducing calorie intake by 500–1,000 kcal/day.
- *Physical Activity:* Moderate activity—brisk walking or jogging.
- *Adjunctive Pharmacotherapy:* Drug treatment for patients with BMI 27 with other medical comorbidities.
- *Surgery:* As the last choice when other modalities fail, BMI 40 or between 35–40 with comorbidities.

Management Recommendations According to BMI

- BMI ≤ 27 with or without comorbidities :
  - Lifestyle management with diet, physical activity, behavioral modification
  - Pharmacotherapy not used
- BMI 27 and ≤ 30 without comorbidities:
  - Same as above
  - Pharmacotherapy can be given
- BMI 27 and ≤ 30 with comorbidities:
  - Pharmacotherapy and lifestyle changes.
- BMI 30:
  - Surgery

Obesity and Pregnancy

- Women of childbearing age with a BMI 30 kg/m^2 or greater should receive information and advice about risks of obesity during pregnancy and childbirth and should be supported to lose weight in between pregnancies in line with NICE Guidelines (No. 189).
- Women to be informed that loss between pregnancies reduces risks of stillbirth, hypertensive complications, macrosomia.
- Pre-pregnancy weight loss with a multi-pronged approach consisting of nutritional modification along with aerobic and strength-conditioning exercises should be the first-line approach.
- Weight loss during pregnancy is not recommended.
- Women with a booking BMI of 40 kg/m^2 or greater to be referred to an anesthetist prior to delivery for assessment regarding difficulties with venous access and regional and general anesthesia.
- Women with more than one moderate risk factor (BMI of 35 kg/m^2 or greater, first pregnancy maternal age of more than 40 years, family H/O of pre-eclampsia, and multiple pregnancy) may benefit from taking 150 mg aspirin daily from 12 weeks of gestation till birth.[21]
- Bariatric surgery is suggested in women with BMI above 32.5 kg/m^2 with comorbidities, and in women with BMI above 37.5 kg/m^2 without comorbidities. Pregnancy should be avoided for at least 12–18 months after the surgery.

Bottom Line

- Prevalence of obesity has doubled in the last few years, so also the health problems associated with it.
- Obesity in women can result in hyperandrogenism, PCOS, adverse reproductive outcome, other metabolic comorbidities like DM, HT.

- Lifestyle changes, healthy diet, and exercise are the need of the hour to stop this epidemic and reduce the health risks.
- Body fat is reasonably indicated by BMI in both adults and children, but it is not measured directly while calculating the BMI. So, instead of using BMI as a diagnostic tool, it should be used as a screening tool to track weight status in the general population. Genetics, physical fat distribution, and fitness level of an individual should be taken into account when assessing the death risk due to potential weight problems.

Conclusion

BMI is an important parameter to assess health of an individual. It is essential to calculate BMI of any patient when we are treating them to understand their current life standard and advice accordingly. New set of diseases like PCOS, Infertility, DM, Atherosclerosis, etc. are emerging due to incorrect lifestyle habits and are plaguing our communities. Correct assessments by various tools are essential to give correct treatment advice to the patients. Various factors such as Genetic, Psychological, Lifestyle, and Economical Factors are responsible and need to be understood well during history taking. Treatment should include multimodal approach to the problems such as managing behavioral strategies, controlling dietary intake, advising physical activities, some amount of pharmacotherapy, and surgeries if required. Women of childbearing age with a BMI 30 kg/m^2 or greater should receive information and advice about risks of obesity during pregnancy and childbirth and should be supported to lose weight in between pregnancies in line with NICE Guidelines. Women with a booking BMI of 40 kg/m^2 or greater to be referred to an anesthetist prior to delivery for assessment regarding difficulties with venous access and regional and general anesthesia. Instead of using BMI as a diagnostic tool, it should be used as a screening tool to track weight status in the general population.

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Chapter 6

Essentials of Micronutrients

Pratibha Singh, Shehla Jamal

Introduction

An increased interest in essential nutrients role in optimizing health and in the prevention or treatment of disease. This explained partly by the increase in knowledge and comprehension of the biochemical functions of these nutrients. It is worth considering few aspects of the discovery of micronutrients. These were all discovered because of deficiency states that occurred in different parts of the world. These could be cured by supplements, firstly of foods, and then of the active chemical component once it had been purified. An instance of these well known are outlined in all textbooks of nutrition, but would include thiamine and beri beri, iodine and cretinism, and of course vitamin C and scurvy. Doctors and other health professionals must be aware of the evidence for the nutritional importance of these substances, and for the conditions where an increased intake may lead to clinical benefit.

What Are Essential Nutrients?

Nutrient: A dietary component that can be utilized by the body to remain healthy. Our body creates many nutrients **(Fig. 1)** on its own, but those it cannot make are called "essential." Most micronutrients are essential and

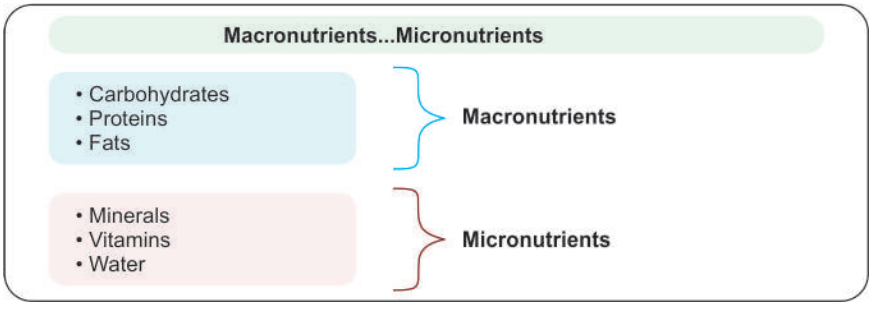

Fig. 1: Categories of macro and micro nutrients

can only be supplied from our food. In contrast, most macronutrients are not essential because they can be supplied by both food and the body. Like, you can eat a carbohydrate as energy foods but, when that energy source runs out, your body can convert fat into carbohydrate to get more energy. Since our body cannot synthesize these micronutrients humans must obtain these from food. Hence, these are also referred to as Essential Nutrients.

Types of Micronutrients

There are four main categories of vitamins and minerals:

- Water-soluble vitamins,
- Fat-soluble vitamins,
- Macrominerals, and
- Trace minerals.

Each micronutrient has a specific function in enabling bodily processes. They are the essential components for muscles, tissues, and bones. They fight infection and take part in chemical/enzymatic reactions & also serve as antioxidants. Since, they cannot be synthesized in the body, they must be taken in the diet regularly. Micronutrient deficiency (hidden hunger) is detrimental to Growth, Immunity, and Health.

Vitamins

They are organic substances required in little amounts to support normal growth and functioning and to regulate metabolism.

Water-soluble: (B and C group) They have to be taken with water, they are not deposited in the body and when taken in excess they get flushed out with urine so, need daily replacement. They are also easily destroyed in bright light, over washing, and overcooking.

Fat-soluble: (ADEK group) They are best absorbed when taken with fat and do not dissolve in water. Excess vitamins will be stored in the liver/fatty tissue and eliminated more slowly than water-soluble vitamins. Also they are not or less sensitive to cooking.

Water-Soluble Vitamins

Most vitamins are water soluble, and hence they are called water-soluble. They're not easily deposited in your body and when taken in excess they get excreted with urine. While each water-soluble vitamin has a distinctive role, their functions are related. For example, most B vitamins act as coenzymes that help in triggering main chemical reactions. A lot of these reactions are necessary for energy production **(Table 1)**.

TABEL 1 **Recommended dietary allowances and sources of water-soluble vitamins**

Nutrient	*Sources*	*RDA (adults > 19 years)*
Vitamin B1 (thiamine)	Fish, meat, whole grain	1.1–1.2 mg
Vitamin B2 (riboflavin)	Milk, eggs, Organ meats	1.1–1.3 mg
Vitamin B3 (niacin)	Leafy greens, beans, meat, salmon,	14–16 mg
Vitamin B5 (pantothenic acid)	Tuna, avocado, organ meats, mushrooms	5 mg
Vitamin B6 (pyridoxine)	Potatoes, carrots, Fish, milk,	1.3 mg
Vitamin B7 (biotin)	Sweet potatoes, eggs, almonds, spinach	30 mcg
Vitamin B9 (folate)	Spinach, asparagus, beef, liver, black-eyed peas	400 mg
Vitamin B12 (cobalamin)	Clams, fish, meat	2.4 mcg
Vitamin C (ascorbic acid)	Citrus fruits, bell peppers, Brussels sprouts	75–90 mg

Various water-soluble vitamins and their function:

- *Vitamin B1 (thiamine):* Aid in converting nutrients into energy.
- *Vitamin B2 (riboflavin):* Essential for energy production, fat metabolism, and cell function.
- *Vitamin B3 (niacin):* Manage the synthesis of energy from food.
- *Vitamin B5 (pantothenic acid):* Essential for fatty acid production.
- *Vitamin B6 (pyridoxine):* Assist your body to release sugar from the deposited carbohydrates for energy and create red blood cells.
- *Vitamin B7 (biotin):* Take part in the metabolism of amino acids, fatty acids, and glucose.
- *Vitamin B9 (folate):* Essential for regular cell division.
- *Vitamin B12 (cobalamin):* Needed for red blood cell formation and help in the nervous system and brain function.
- *Vitamin C (ascorbic acid):* Needed for the synthesis of neurotransmitters and collagen, the chief protein in your skin.

Vitamin B Complex and C Deficiencies

- B1-Thiamin—Beriberi nervous system deterioration b/c use of milled rice.
- B2-Riboflavin—Poor wound healing, breakdown of tissue in mouth/nose
- B3-Niacin Pellagra—Affects skin, intestines, and brain
- B6-Pyridoxine—Anemia, nervous/muscle disorders

- B9-Folic Acid—Anemia, birth defects (Spina Bifida, brain damage), Associated with depression, dementia, cardiovascular disease
- B12-Cobalamin—Anemia relies on intrinsic factor from the stomach for absorption
- Vit—C Ascorbic Acid Scurvy

Fat-Soluble Vitamins

They do not dissolve in water are best absorbed when taken with fat **(Table 2)**. After utilization, these vitamins are deposited in our liver/fatty tissues for later use.

The details of these vitamins are:

- *Vitamin A:* Essential for proper vision and organ function
- *Vitamin D:* Helps in calcium absorption and bone growth and aid in proper immune function
- *Vitamin E:* Helps in immune function and acts as an antioxidant that defends cells from damage
- *Vitamin K:* Needed for blood clotting and appropriate bone development

TABLE 2 **Recommended dietary allowances and sources of fat-soluble vitamins**

Nutrient	*Sources*	*RDA or AI (adults > 19 years)*
Vitamin A	Retinol (liver, dairy, fish), carotenoids (sweet potatoes, carrots, spinach)	700–900 mcg
Vitamin D	Sunlight, fish oil, milk	600–800 IU
Vitamin E	Sunflower seeds, wheat germ, almonds	15 mg
Vitamin K	Leafy greens, soybeans, pumpkin	90–120 mcg

Vitamin A

Deficiency

- Ocular change
- Night blindness
- Xerophthalmia
- Extraocular changes
- Growth retardation
- Acquired immune deficiency
- Increased risk of infections
- Rough, dry skin, Acne
- Poor functioning of lungs and digestive tract

Toxic Effects

Very high amounts 50,000 IU/day for long can cause:

- Poisoning
- Hepatosplenomegaly
- Birth defects
- Fatigue, malaise
- Anorexia, vomiting

Vitamin D

Deficiency

- Rickets
- Osteomalacia
- Osteoporosis

Toxic Effects

- Hypervitaminosis
- Hypercalcemia
- Hyperphosphatemia
- Hypertension which manifests as nausea and vomiting
- Excessive thirst and polyuria, severe itching
- Joint and muscle pains
- Azotemia
- Nephrolithiasis, ectopic calcification
- Disorientation & coma

Macrominerals

These are required in high amounts than trace minerals to carry out their distinct roles in the body **(Table 3)**. The macrominerals and their functions are:

- *Calcium:* Essential for proper formation and function of bones and teeth. Aid in blood vessel contraction and muscle function.
- *Phosphorus:* Part of the cell membrane and bone structure.
- *Magnesium:* Helps with over 300 enzyme reactions, together with control of blood pressure.
- *Sodium:* Electrolyte that helps in fluid balance and regulation of the blood pressure.
- *Chloride:* Frequently found in combination with sodium. Assists in maintaining the fluid balance and is used to produce digestive juices.

- *Potassium:* Electrolyte that regulates fluid status in cells and aids in muscle function and nerve transmission.
- *Sulfur:* Present, in every part of living tissue and present in the amino acids methionine and cysteine.

TABLE 3 **Recommended dietary allowances and sources of macrominerals**

Nutrient	*Sources*	*RDA or AI (adults > 19 years)*
Calcium	Broccoli, milk products, leafy greens	2,000–2,500 mg
Phosphorus	Turkey, salmon, yogurt	700 mg
Magnesium	Black beans, almonds, cashews	310–420 mg
Sodium	Canned soup, salt, processed foods	2,300 mg
Chloride	Celery, seaweed, salt	1,800–2,300 mg
Potassium	Bananas, lentils, acorn squash	4,700 mg
Sulfur	Garlic, onions, Brussels sprouts, eggs, mineral water	None established

Trace Minerals

Trace minerals are required in lesser amounts than macrominerals, however, it still enables essential functions in your body **(Table 4)**. Trace minerals and their functions:

Iron: Helps in providing oxygen to muscles and aid in the production of certain hormones.

Manganese: Helps in amino acid, carbohydrate, and cholesterol metabolism.

TABLE 4 **Recommended intakes of trace minerals and sources**

Nutrient	*Sources*	*RDA or AI (adults > 19 years)*
Iron	Oysters, white beans, spinach	8–18 mg
Manganese	Pineapple, pecans, peanuts	1.8–2.3 mg
Copper	Liver, crabs, cashews	900 mcg
Zinc	Oysters, crab, chickpeas	8–11 mg
Iodine	Seaweed, cod, yogurt	150 mcg
Fluoride	Fruit juice, water, crab	3–4 mg
Selenium	Brazil nuts, sardines, ham	55 mcg

Copper: Important for connective tissue genesis, along with normal brain and the nervous system function.

Zinc: Essential for immune function, normal growth, and wound healing.

Iodine: Helps in thyroid regulation.

Fluoride: Requires for the growth of bones and teeth.

Selenium: Essential for thyroid health, reproduction, and protection against oxidative damage.

Macro- and Microminerals Deficiencies

- Calcium and magnesium—Tetany-muscle cramps, numbness, and tingling in limbs. Rickets and osteoporosis–chronic deficiency.
- Zinc—Develops as a part of malnutrition or malabsorption syndrome due to low intake or intestinal disease, can also affect CNS.
- Iodine—During pregnancy, it can result in stillbirth, spontaneous abortion, congenital abnormalities such as cretinism, increased PNM, and goiter.
- Iron—Anemia leads to reduced disease resistance and poor growth and development.

Water

Water is essential to human life. Role of water is to:

- Stimulate the kidneys to remove toxins.
- Transport nutrients and other body substances.
- Help to regulating body temperature.
- Help in digestion, absorption.
- Help to keep skin and muscle toned.

Healthy Balanced Diet

It is essential to eat food from each group daily. Nutrient requirements vary depending on:

- Age
- Gender
- Physical activity
- Pregnancy
- Breastfeeding
- A healthy balanced diet provides adequate food for energy and nutrients **(Fig. 2)**.

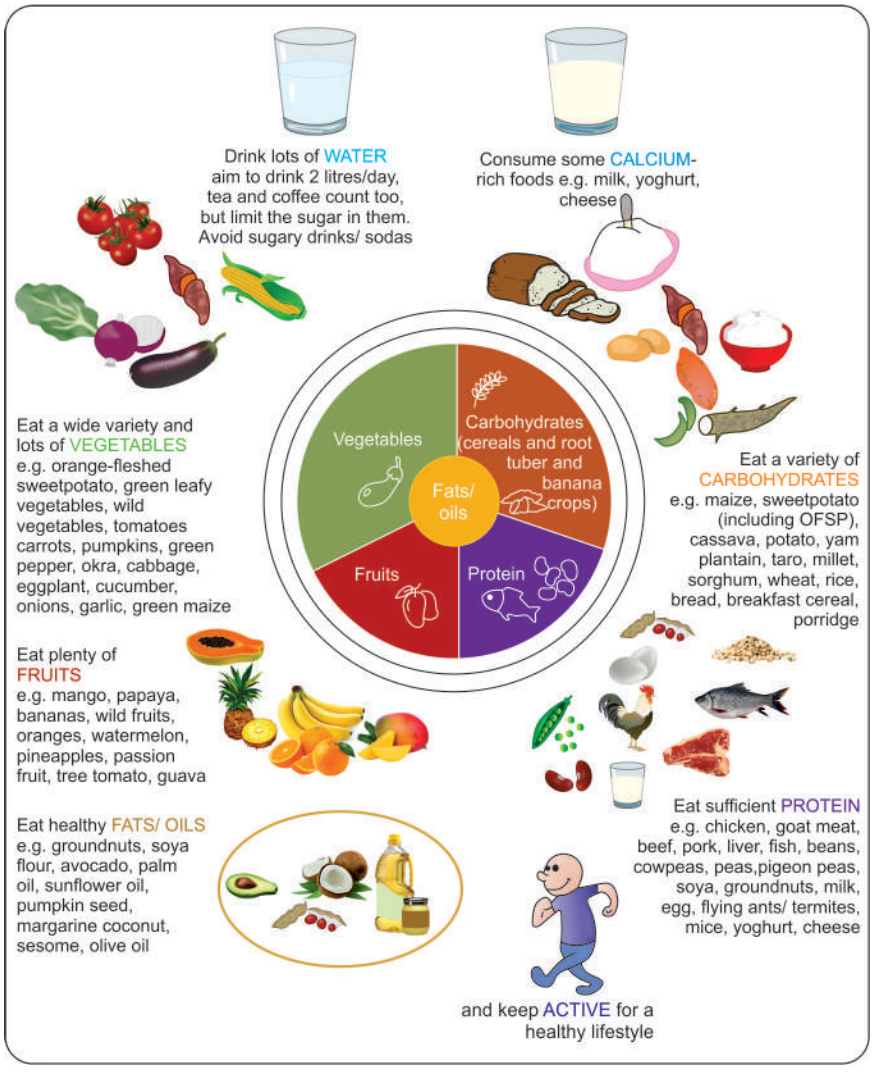

Fig. 2: Healthy balanced diet

Micronutrients Health Benefits

Although we only need micronutrients in micro amounts, but they are vital and deficiency of these can cause serious health problems. So they are mandatory for:

- the adequate functioning of the body,
- may even provide immunity to fight against disease,
- also act as antioxidants, and
- may provide immunity to fight against diseases like cancer, Alzheimer's, and heart disease.

Micronutrient Deficiencies

An inadequate amounts of these micronutrients can lead to negative side effects. Most of the healthy adults can get an appropriate amount of micronutrients from a balanced diet but there are also certain populations who are affected due to a lack of proper vitamins.

These include:

- *Vitamin D:* Approximately 77% of Americans are deficient in vitamin D, mostly due to lack of sun exposure.
- *Vitamin B12:* Vegans and vegetarians may affect by vitamin B12 deficiency with abstain from animal products. Elderly individuals are also affected by less absorption of vitamins with age.
- There is also a lack of vitamin A in most of the women and children in the developing countries.
- Lack of Iron is commonly shown among preschool children and menstruating women.
- There is also a lack of Calcium in almost 22% of men and 10% of women who are above 50 years old.

Tackling Micronutrient Malnutrition

See **Figure 3**.

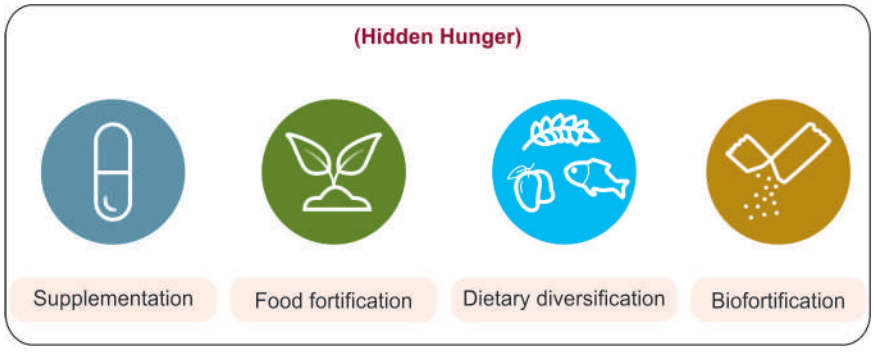

Fig. 3: Tackling micronutrient malnutrition

Supplementation

Taking a capsule or injection containing a sufficient amount of the deficient micronutrient **(Fig. 4)**.

Food Fortification

Adding an essential micronutrient to commonly consumed processed foods such as cooking oil, sugar, salt, and flour.

Fig. 4: Micronutrient supplementation

Dietary Diversification

Increasing the variety and amount of micronutrient-rich foods, with social and behavior change activities, so that there is increased production or access to nutrient-rich foods.

Biofortification

Breeding varieties of a popular staple food crop with high amounts of at least one important micronutrient.

Micronutrient Toxicities

Micronutrient toxicities are infrequent than deficiencies. They are potentially to occur with large doses of the fat-soluble vitamins A, D, E, and K, since these can be stored in the liver and fatty tissues & cannot be eliminated from the body like water-soluble vitamins. Micronutrient toxicity generally develops from supplementing with excess amounts—rarely from food sources. It is also essential to know that excessive consumption of certain nutrients can still be dangerous even if it does not lead to overt toxicity symptoms.

Conclusion

Deficiencies of micronutrients are a major global health problem, and 2 billion people in the world today are estimated to be deficient in key vitamins and minerals like vitamin A, iodine, iron, and zinc. Micronutrients play a central part in metabolism and in the maintenance of tissue function. Since our body needs micronutrients in

specified amounts, deficit and surpluses of any one nutrient cause negative issues. Single micronutrient deficiency can easily be recognized and treated. Subclinical & multiple micronutrients deficiency is more difficult to recognize. Diet-related deficiencies do occur in vegans, the elderly, and the alcoholics. An adequate intake is necessary, but excess supplements to people who do not need them may be harmful.

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Chapter 7

DHA—A Key Nutrient

Monika Gupta, Vidya Thobbi

Introduction

Fats are essential for all organisms. Fatty acid (FA) has a variable length carbon chain with a methyl end and a carboxylic acid head. FAs can be classified based on the degree of saturation of their carbon chains. Saturated FAs have the maximum number of hydrogen atoms, while monounsaturated FAs have one, polyunsaturated FAs (PUFAs) have two or more, double bonds.[1]

Polyunsaturated FAs received from diet are necessary for various physiological processes; however, they cannot be produced in body and they need to be incorporated in diet. These are also called essential FAs. PUFA have a role in the following conditions:[2]

- Cardiovascular diseases
- Rheumatoid arthritis
- Neuropsychiatric diseases
- Inflammation
- Obesity

There are two types of polyunsaturated FAs **(Table 1)**:

- Omega-3—Alpha-linolenic acid (ALA) is a parent omega-3 FA.
- Omega-6—Linolenic acid (LA) is a parent omega-6 FA.

Essential FAs are metabolized to long chain FA and form its metabolites. These metabolites are active and have physiological actions.[3]

TABLE 1 **Various types of Polyunsaturated Fatty Acids**

Omega-3 FAs	*Omega-6 FAs*
• Alpha-linolenic acid • Ecosapatothenic acid • Docosapentaenoic acid • Docosahexaenoic acid	• Linoleic acid • Gamma-linolenic acid • Diho-gamma- linolenic acid • Arachidonic acid • Adrenic acid

Docosahexaenoic Acid (DHA)

DHA is synthesized primarily in endoplasmic reticulum of liver from ALA. DHA is one of the most important omega-3 FA as it constitutes 10–20% of total lipids in brain. DHA is stored in phospholipid membranes and structures like synaptic terminus, mitochondria, and endoplasmic reticulum. Thus it is believed that DHA affects various cellular characteristics and physiological activities comprising membrane fluidity, transmembrane receptor function, gene expression, release of neurotransmitter, signal transduction, lipid raft function, myelination, neuroinflammation, and neuronal differentiation and growth. Due to variety of functions, DHA has key role in throughout human life-stages.[4]

Sources of DHA

The primary source of omega FAs are vegetable oils including sunflower oil, safflower oil, sesame oil, palmolein oil, and corn oil. About 10–15% of omega-6 FAs are obtained as a fundamental component of cereals, pulses, tubers, legumes, and vegetables as "invisible fat". Omega-3 FAs are available in abundance in dietary sources like vegetable oils like flaxseed or linseed oil, rapeseed or canola oil, peanut oil, olive oil, soya oil, walnut oil, green leafy vegetables, fenugreek seeds, kidney beans, dry fruits, oily cold-water, fish and fish oil.[3]

Different Functions of DHA in Body

DHA is essential in initial growth and development of brain in infants and also maintenance of normal brain in adults. Along with DHA's role in nervous system it also has role in multiple other organ systems and diseases **(Table 2)** as mentioned below:[5]

- Cardiovascular disease
- Cancer
- Inflammation
- Asthma
- Immunity

Importance of DHA throughout Life Stages

Humans require essential FAs for all physiological processes like growth, development, and the maintenance of cellular functions necessary to life. In the below section role of DHA during entire course the human life cycle is summarized.

Fetal and Neonatal Development

Fetal development is characterized by period of and rapid growth represents growth and metabolic turnover in the life stages of human. During this period

TABLE 2 **Organ system and role of DHA**

Diseases	*Role of DHA*
Nervous system—Infant	• Maintenance of normal neural functions • Dominant structural FA in the brain gray matter and retina
Nervous system—Adult	• Maintenance of the brain and of learning during aging • Ameliorates the learning performance failure caused by cholinergic dysfunction • Maintenance of the cognitive functions of the brain • Neuronal protection in the CNS
Cardiovascular diseases	• DHA supplements increase the HDLrLDL cholesterol ratio and decrease the total cholesterol HDL ratio, suggesting a decreased risk for coronary artery disease. • DHA may have a role in preventing severe arrhythmias in myocardial ischemia
Cancer	• DHA supplementation may be advantageous in adjuvant chemotherapy
Inflammation	• EPA and DHA have anti-inflammatory properties and may change lymphocyte, monocyte, and macrophage functions
Immunity	• Omega-3 to omega-6 long-chain FAs in the diet may modulate the host response to respiratory infection with less infection correlated with a higher level of omega-3 FAs

weight of human brain increases 60 fold from 2nd trimester to 2 years of age. Among omega-3 FAs, DHA is present in abundance in the brain and retina, and constitutes approximately 50% weight of neuronal plasma membranes. DHA improves cell membranes fluidity and regulates physiology of neurotransmission, including signal transduction by acetylcholine, dopamine, and serotonin, and has major effect on cognition, vision, and behavior.[6]

Childhood

Limited evidence is available on the association between consumption of FA and health outcomes in children above 2 years. Nonetheless, it is well recognized fact that an optimal intake of DHA is necessary for Child's normal growth and development as well as cognitive development.[6] A study was conducted on children aged 5 years whose mothers were supplemented with 200 mg/d of DHA while lactation and from delivery until 4 months post delivery, which showed that these children performed better on attention tasks than children whose mothers were supplemented with vegetable oil.[7] DHA has also been effective in management of childhood diseases like attention-deficit hyperactivity disorder,[8] upper respiratory illness, and allergy.[9]

Adulthood

In adults, Suboptimal intake of omega-3 FAs has been linked with many diseases including cardiovascular, inflammatory/autoimmune, neurodevelopmental, and psychiatric disorders.[10,11] A study was conducted in 280 adult volunteers without neuropsychiatry diseases and they assessed cognitive functions, and it was found that higher levels of serum DHA to be related with significant improvement in nonverbal reasoning and mental flexibility, working memory, and vocabulary.[11] It is also suggested that, in adults dietary intake of omega-3 FAs is associated with protective action on endothelial function.[12]

Advanced Age

The aging is physiological process that leads to decline in functional and physiological processes that lead to change in nutritional needs in the ageing population. In the ageing population, omega-3 FAs have effects like inhibit hepatic triglyceride synthesis, decrease inflammation, and inhibit platelet aggregation.[13] DHA supplementation is also being associated with neuroprotective effects.[14] Moreover, oxidation of DHA activates neuroprostanes and neurofurans, which are effective anti-inflammatory metabolites similar to prostaglandins which have a role in maintaining brain health in elderly population.[15,16]

DHA in Pregnancy and Lactation

Diet and lifestyle are important determinants of health of both mother and offspring, starting from the preconception period. During pregnancy, the quality of fats is more important than their total amount, especially for fetal development and infant growth. For this reason, it is necessary to improve the relative proportion of polyunsaturated fats rather than to increase the intake of total fats: an optimal intake of DHA is necessary for the growth and development of brain and retina.[17] Among polyunsaturated FAs in brain and retina DHA is the predominant component. And hence is necessary during pregnancy for brain and retinal development of the fetus. It is also well known that DHA plays major roles in the psychomotor neurodevelopment in the first months of life, when it is supplied at high amounts by breastmilk.[18]

Benefits of DHA to Mother

Multiple maternal benefits have been suggested with DHA supplementation in pregnant women. DHA supplementation in initial stage of pregnancy could decrease the occurrence of placental disorders. In the failure of a normal placentation may lead to complication of uteroplacental ischemia which further leads to several complications such as preeclampsia, fetal

growth restriction, preterm labor, and PROM.[19] In one of the review which evaluated the effects of DHA supplementation in prevention of placental disorders, this study concluded that supplementation of DHA in first trimester was associated with better outcome.[20] Preeclampsia is another obstetrical complication caused due to placental dysfunction. This can be attributed to combination of extreme oxidative stress and endothelial dysfunction.[20] In one of the study conducted they evaluated levels of serum FA concentrations in women with preeclampsia and it showed that low levels of DHA in maternal plasma, cord plasma, and placenta of preeclampsia women.[21] Results of this study is disputable, as in one of the Systematic review by Cochrane showed that there is not enough evidence to support the use of marine oil supplementation in order to reduce the rate of preeclampsia.[22] In obese pregnant women obstetrician have concern because of the increased risk of maternal and fetal morbidity. A review conducted recently studied the effect of poly unsaturated FAs in obese pregnant women associate with metabolic syndrome. This study concluded that PUFAs supplementation provide benefits, which include prevention of preterm labor and preterm birth and also improvement in fetal and neonatal outcome in obese pregnant women.[23] Gestational diabetes mellitus (GDM) is another common complication encountered in pregnancy with rising prevalence of 3% and 10%. GDM is responsible for short- as well as long-term maternal and fetal morbidity. The corelation between DHA supplementation and incidence and severity of GDM has been studied. The DOMInO trial showed that a daily supplementation of 800 mg during the second trimester was unable to reduce the risk of GDM. Non the less in the DHA treated group there was a significant effect on perinatal mortality and neonatal convulsions.[24] Lower serum PUFA levels were associated with major depression.[25] In last trimester of pregnancy there is physiological depletion of PUFA can be correlated with an increased incidence of postpartum depression. A retrospective observational study conducted compared women having postpartum depression and controls this study showed that lower serum PUFA levels in the postpartum depression group and implied that there is possible benefit of a DHA supplementation.[26] Another study reported that decreased ratio of DHA to omega-6 FAs is associated with the increased risk of postpartum depression.[27]

Benefits of DHA to Fetus

Fetal growth depends on the normal functioning placenta and an optimal nutritional status of mother. Low birth (LB) weight infant are at high risk of short-term as well as long-term morbidity and mortality. Several studies have shown the effectiveness of DHA supplementation on weight of newborn. A small randomized controlled study conducted on 43 women who were

at high risk for preterm delivery. In this study they evaluated the effect of vaginally administered DHA versus placebo. In women supplemented with DHA had a significant increase in gestational age at delivery and in newborn birth weight.[28] In another prospective study conducted concluded that a positive association amongst maternal DHA concentrations and birth weight.[29] In another double blind controlled study including 350 women who received either 600 mg/d DHA or placebo, this study concluded that DHA supplementation in the last half of pregnancy was associated with overall increased gestation duration and infant size.[30] Intrauterine growth restriction (IUGR) is a complex disorder. When IUGR is linked to placental insufficiency, fetal lipid metabolism may be adversely affected. Several animal studies have reported an damaged DHA transplacental transfer in IUGR. This could be one of the reasons for the neurological symptoms linked to IUGR.[31] In a prospective study including pregnant women, DHA concentration of maternal erythrocyte in first trimester was linked with weight of neonates. Also in women who delivered low birth it was found that DHA levels were found to be low compared to controls.[32] DHA is important to fetal, neural, and retinal development. Evidences available till now concludes that optimal DHA levels in mother may provide certain benefits for child's neurodevelopment. Moreover, DHA is considered to be safe, with no adverse birth outcomes which can be correlated to DHA supplementation.[33]

Multiple governing bodies are recommending supplementation of DHA during pregnancy and lactation **(Table 3)**.

TABLE 3 **Recommendations for DHA supplementation in pregnancy**

Authority	*Adults (DHA mg/day)*	*Pregnancy (DHA mg/day)*	*Year*
European food safety authority	250	250	2012
Nordic Nutrition Recommendations (NNR)	200–250	200	2012
WHO	200–1000/Week	—	2003
National Health and Medical Research Council	430–610	115	2006

Conclusion

In multiple studies it is concluded that there is increased need of DHA in pregnancy and a possible depletion of maternal source of DHA. It is evident that DHA is an important nutrient for the several physiological processess, especially

during pregnancy and lactation. The benefits of DHA can be correlated to its anti-inflammatory and anti-oxidative properties placental blood flow as well as amniotic membranes resistance. It is clear that during the last trimester, maternal serum DHA concentrations are decreased, which is believed to be because of vascular volume extension and maternal, placental, and fetal DHA increased requirements. Many studies reported adverse outcomes in pregnancy linked to low-serum levels of PUFA. An increased dietary fat intake should be recommended during pregnancy. There is no clear understanding on the efficacy of a DHA supplementation however multiple studies do support a preventive effect of DHA. DHA should be prescribed in patients with a low-dietary intake and risk factors. It is a safe supplementation with minimal side effects.

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Chapter 8

Nutrition in FGR

Jayanthy T, Sindu KS

Introduction

Low birth weight is a major problem in India with 3 million LBW babies born annually (Incidence: 15–25%). FGR accounts for 30% of stillbirths. Malnourished mother will have IUGR baby. Nutrition has a role in development and expression of fetal genome. Fetal origin of adult disease is well known and the intrauterine environment may affect the baby and cause metabolic, endocrine, and cardiovascular disease later in life. Placenta is essential in maintaining fetal growth. Any alteration in placental structure or function leads to FGR. Placental insufficiency is multifactorial. Nutrient transport through the placenta is directly dependent on the thickness of exchange barrier, uteroplacental perfusion and transporter concentration and capacity. The placenta has an array of nutrient sensing signaling pathways, which act in a coordinated way to regulate nutrient uptake and cellular signaling in response to maternal supply and fetal demand.[4]

O-linked N-acetylglucosamine transferase (OGT) are the primary nutrient-sensing proteins in glucose and amino acids utilization and signaling. Glucose, amino acids, and oxygen are the major nutritional substrates utilized for fetalgrowth.[2]

WHO Classified Malnutrition

- Undernutrition
- Micronutrient-related malnutrition
  - micronutrient deficiencies,
  - micronutrient excess.
- Overweight, Obesity

Daily requirement:

Protein	61–70 g/day
Fat	60–85 g/day
Fiber	25 g/day

First Trimester

Mainly organogenesis and fetal programming for further growth. Critical nutrients required include protein, folic acid, vitamin B12, and zinc.

Second and Third Trimesters

Maximum fetal growth (90%) is seen in later part of gestation, so nutrion is very important at this stage. Critical nutrients required are protein, iron, calcium, magnesium, vitamin B and omega 3 fatty acid, and docosahexaenoic acid.

Energy Requiments during Pregnancy

Energy requirement depends on age, body size, pre-pregnancy weight, and lifestyles.

Additional energy needs for normal weight women:

- 2nd trimester + 360 kcal
- 3rd trimester + 470 kcal
- Lactation + 500 kcal

For growth and development of fetus glucose is essential. Glucose is transported across the placenta by sodium independent facilitated diffusion by the GLUT family of transporter located on the basal side of the membrane. GLUT receptor expression steadily increases throughout gestation. Empty calorie means high energy foods with little nutritional values, e.g., added sugars (soft drinks, puddings, ice creams, sweet juices), solid fats (oily foods, cheese, whole milk, and fatty meats). Avoid such foods.

Protein Reqirements

Pregnancy and Lactation—55 g + 20 g

Dietary Sources

- Red meat liver, poultry, fish, eggs, and milk
- Vegetarians—soybeans, milk, soy products, dry beans, nuts

Precaution

- Commercial protein supplements are not recommended.
- Complete proteins—proteins from meat, poultry, fish, eggs, milk, cheese, yoghurt provide all nine essential amino acids.
- Incomplete proteins—vegetables, grains, nuts, seeds, legumes lack one or more essential amino acids.
- The native 'Dal-Roti' Rice—Sambar combination supplements each other rather well, while cereals lack in amino acids (lysine and threonine)

legumes lack in amino acids (methionine and tryptophan), when taken together they cover up the deficit of each other.

Nutritional Causes

- BMI—20 kg/m^2
- BMI—30 kg/m^2
- Intense daily exercise
- Low fruit intake
- Severe anemia
- Undernutrition/Malnutrition
- Inflammatory bowel disease
- Intestinal bypass surgery

Role of Nitric Oxide in FGR

Uteroplacental vasculature in normal pregnancy is—low resistance and high flow which depend on nitric oxide bioavailability. In vivo NO is obtained by oxidation of L-arginine by NO synthase. NOS enzymes require oxygen for the synthesis of Nitric Oxide. Impaired placental synthesis of nitric oxide may provide an explanation for FGR. In uteroplacental insufficiency amino acid supplementation may not be effective.

L-arginine in IUGR (Flowcharts 1 and 2)

L-arginine is required for NOS enzyme but arginine undergoes rapid metabolism in liver and GIT. L-citrulline supplementation was tried but in hypoxia it is not useful as enzyme function is reduced.[5]

Studies by Cynober (2007) and Romero et al. (2006) amino acid supplementation with L-arginine or l citrulline was ineffective when hypoxia was present. The arginine group 1.042 kgs vs. placebo group 1.068 kg.

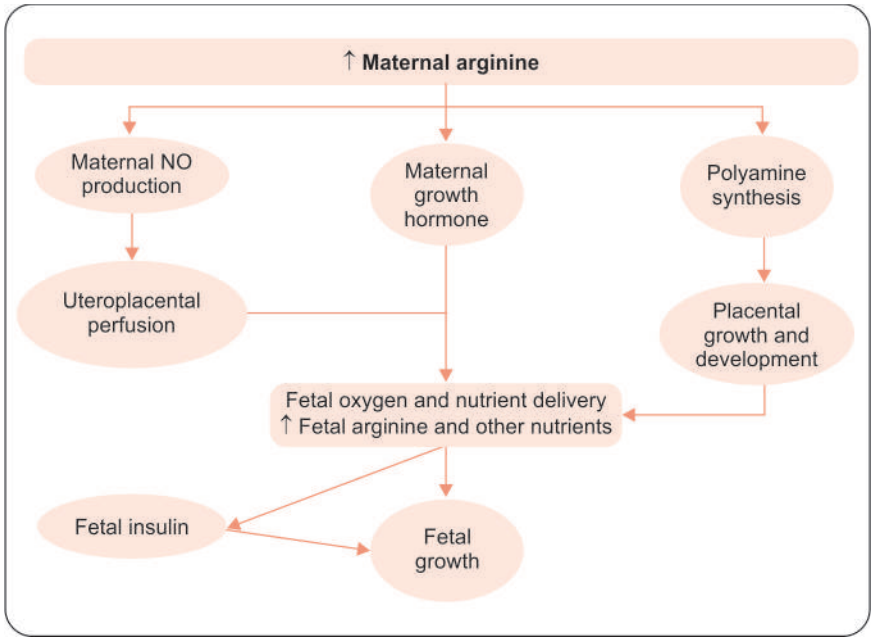
Fat

- Recommendation for pregnancy 20–30%
- 2nd trimester 54–82 g/day
- 3rd trimester 57–85 g/day
- Saturated fat 10%, Monosaturated fat 12–15%, Polysaturated fat 5–7%
- One should be aware that fats are completely absorbed during pregnancy causing marked increase in serum lipids and cholesterol

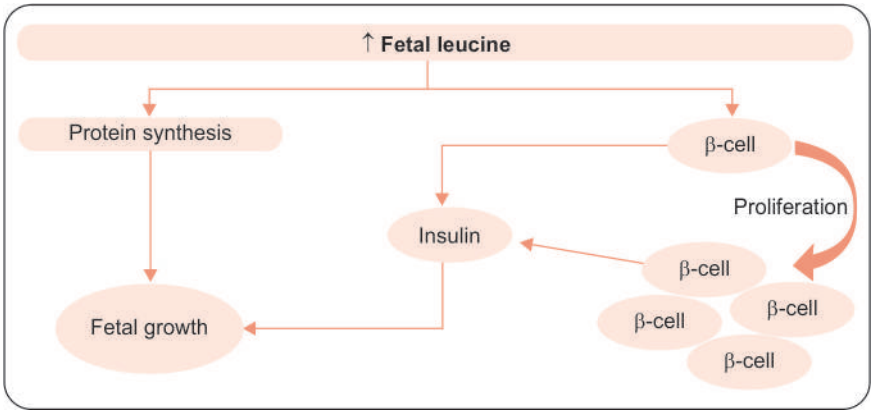
Role of Fatty Acids in FGR

Adequate consumption of omega-3 fatty acids, which are essential fatty acids, are important during pregnancy as they are critical building blocks of

Flowchart 1: Mechanism by which arginine might improve fetal growth[9]



Flowchart 2: Mechanism by which leucine might improve fetal growth[9]



fetal brain and retina. Fish and other seafood contain long-chain omega-3 polyunsaturated fatty acids (PUFA), which are essential nutrients. The most biologically active forms are omega-3 fatty acids are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). A period of dynamic structural neural growth occurs in the fetal brain during the third trimester.

Consensus guidelines have recommended at least 200 mg of DHA per day.[2,3] Good sources of omega 3 fatty acids—flaxseed oil (50–60% ALA),

Iron

Heme iron (25% absorption) AA	Non-Heme iron (25% absorption)
Fish/seafood	Dark green leafy vegetables (spinach and kangkung)
Meat (beef/lamb/pork)	Legumes (bean, dried fruits, and seed)
Poultry	Eggs

canola oil, raeseed oil (11% ALA), soybean oil, deep sea scolded fish, omega 3 enriched eggs, pulses (beans, dhal), nuts/seed.

ICMR 2009 Micronutrients Requirement in Pregnancy

Magnesium (310 mg/day), Sodium (2 gm/day), Potassium (3.5 gm/day), Iron (35 mg/day), Zinc (7.3–13 mg/day), Iodine (200 mcg/day).

Vitamin RDA mg/day—Thiamine 1.4, Riboflavin 1.4, Niacin 16, B6 2.5, B12 1.2, C 60 mcg/day, A 800 mcg/day, D 600 IU/day women (Hb ≥ 110 g/L). 30% increased risk for LBW when anemia occurred during the first two.

Recent reviews have identified maternal iron, balanced protein-energy, and multiple micronutrient supplementation as the most effective interventions to alleviate FGR. Providing these interventions before pregnancy or in early months is logistically difficult because in many developing countries, the majority of pregnant women attend antenatal clinics in their second or third trimester.

Indian diet does not provide the required iron and anemic pregnants have a higher chance of preterm deliveries and low birth weight babies. In one of the studies it shown that for every extra 10 mg of iron intake the fetal birth weight increased by 70 gm.[3] So correcting of anemia by supplementing will reduce the risk of low birth weight babies. Correction of anemia is important in 1st and 2nd trimesters to attain adequate fetal growth.

Calcium

Calcium requirement in pregnancy is 1200 mg/day. Diet alone insufficient to meet the requirement supplementation is always necessary. In 19 trials with 8,287 women it was found that those with calcium supplementation had higher birth weight babies compared to placebo.[1]

Folate

RDA-400 mg/day.

Difficult to get 400 mcg of folate through diet alone. Vitamin with folic acid supplements, eating fortified foods, or a combination of the two, in addition to consuming a balanced diet rich in natural food folate. Fortification of foods with folic acid example rice, bread, cereals, and pasta may meet the

requirement. These foods are labeled "enriched." Folic acid is a specific type of folate that does not generally occur naturally.

Zinc[2]

- Maternal and fetal requirement increases in pregnancy
- 1st trimester 5.5 mg
- 2nd trimester 7 mg
- 3rd trimester 10 mg
- Lactation 9.5 mg[2]

Zinc deficiency in pregnancy may cause obstetric complication and fetal malformation. Vegetarians require zinc supplementation Zinc supplementation is recommended when iron supplementation 30 mg/day as large amount of iron supplement decrease zinc absorption. In many of the studies it has been showed that intake of <6 mg/day had a twofold risk of low birth weight babies. Presently there is incomplete data regarding the maternal zinc deficiency and fetal malformations.

Vitamin A

Vitamin A have a role in embryogenesis and fetal growth. Diet alone can meet the requirement supplementation is not required. High doses (25000 IU/3000 ug/day retinol) might relate with birth defects (fetal toxicity).

Vitamin D

Vitamin D helps the body to use the calcium that is consumed, maintain blood calcium and phosphorous levels, and have antiproliferative action. Source of vitamin D sunlight exposure, fish (salmon, tuna, sole), milk, cereal, pork, mushrooms, ricccota cheese, and cod liver oil. The most recent meta-analysis revealed that 25(OH)D insufficiency (37.5 nmol/L) during pregnancy was associated with increased risk for small SGA (OR 1.85; 95% CI 1.52, 2.26, 6 studies). Estimated average requirement for vitamin D during pregnancy is 400 IU/day (10 μg/day). A Cochrane review of three RCTs identified vitamin D treatment alone significant in reducing risk for SGA compared to no supplements/placebo. Currently, there is insufficient evidence to promote the use of a vitamin D supplement (with or without calcium) during pregnancy to reduce the risk of LBW babies.

Vitamin C

Mothers and Children's Environmental Health (MOCEH) study in South Korea to determine whether maternal intake of fruits and vegetables or vitamin C is associated with fetal and infant growth.[7] A total of 1138 Korean

pregnant women at 12–28 weeks gestation was recruited for the MOCEH. Results: A multiple regression analysis after adjusting for covariates showed that maternal intake of fruits and vegetables were associated with higher weight, BPD, AC, and birth length from birth to 6 months. In addition, there was a significant inverse relationship between consumption of fruits and vegetables (below the median compared to above the median of ≥519 g/d).

Iodine[2]

Iodine requirement increases in pregnancy. In pregnancy due to hormonal interaction TSH should be ≤3. Recommendation 200 ug/day.[2] Food sources are seaweed, fish, egg, milk, dried legumes, dried vegetable, and fruits.

Probiotics

Probiotics taken during pregnancy might help lower the risks of pre-eclampsia and premature birth, suggests observational research in the online journal (BMJ Open). Timing of probiotic milk[6] consumption during pregnancy and effects on the incidence of pre-eclampsia and preterm delivery.

Micronutrient Sources

- Milk, cheese, eggs (yolk), orange and yellow fruits and vegetables provide vitamin A.
- Legumes, wholegrain cereals, nuts, seeds, green leafy vegetables provide vitamin B.
- Citrus fruits, broccoli, strawberry, parsley, cabbage provide vitamin C.
- Citrus fruits, broccoli, strawberry, parsley, cabbage provide vitamin D.
- Olives and olive oil, avocado, wholegrain cereals Iron - Lean meat, green leafy vegetables, and legumes provide vitamin E.
- Dairy products, almonds, green leafy vegetables provide calcium.[3]
- Nuts, seeds, whole grains, legumes, green leafy vegetables provide magnesium.[3]
- Lean meat, chicken, fish, sunflower, and pumpkin seeds provide zinc.[3]
- Brazil nuts, wheat germ, sunflower seeds, oats provide selenium.[8]
- Progesterone and calcium have no role in preventing IUGR though used prophylactically in pre-eclampsia.
- TPN has no role except in Hyperemesis and malabsorption.[8]
- Avoiding smoking helps in prevention of IUGR.

Diet Pattern: In a study done in Auckland it was found that women consuming traditional food like fruit, vegetables, yogurt, and lean meat had less incidences of low birth weight babies compared to those who consumed high fat, refined grains, sweets, and processed meat.

Foods to Be Avoided in Pregnancy

Unboiled or unpasteurized milk, raw egg, raw or under cooked meat. Foods that contain high mercury levels like shell fish shark, swordfish, tilefish, and king mackerel to be avoided.

Salmon, trout, pollock, and cat fish are low in mercury can be taken.

Caffeine Intake[2]

- Moderate intake (300 mg for 24 hours) 2–3 servings consumption not linked to adverse effects on pregnancy.
- High intake (500 mg/day) can increases the risk of abortion.
- Coffee reduces the absorption of iron, calcium, and zinc.

Conclusion

Good antenatal care and practices are essential for a healthy fetus. Nutrition plays a major role in fetal growth. Balanced diet with all essential nutrients is impotant. Weight gain should be ideal. Exercise helps not only in maintaing weight but also reduces GDM. Recommended vitamin and mineral supplements to be taken. Harmful substances like alcohol, tobacco, and certain drugs to be avoided. Fresh foods are better than tin/canned foods.

Healthy habits now will give a healthy future generations.

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Chapter 9

Nutritional Deficiency and Anemia

Vidya A Thobbi

Introduction

Anemia is a condition where the number of red blood cells or the hemoglobin concentration within them is lower than normal. Hemoglobin is necessary to carry oxygen and if red blood cells are too few or abnormal or not enough hemoglobin, there will be a decreased capacity of the blood to carry oxygen to the body's tissues. This results in symptoms such as fatigue, weakness, dizziness, shortness of breath, and signs such as tachycardia, pallor, jaundice, koilonychias, splenomegaly, petechiae, ecchymosis, atrophy of tongue papillae, etc. The optimal hemoglobin concentration needed to meet physiologic needs varies by age, sex, elevation of residence, smoking habits, and pregnancy. The most common cause of Anemia is nutritional deficiencies. Other causes include Hemoglobinopathies, infectious diseases such as malaria, tuberculosis, HIV, parasitic infestations, etc. Anemia is a serious global public health problem that particularly affects young children and pregnant women. WHO estimates that 42% of children less than 5 years of age and 40% of pregnant women worldwide and 30% of world's population are anemic.

Classification of Anemia (ICMR)

- Normal: 11 g/dL or higher
- Mild: 10–10.9 g/dL
- Moderate: 7–10 g/dL
- Severe: <7 g/dL
- Very severe: <4 g/dL

Anemia Classification (WHO)

See **Table 1**.

Indian and International Goals

- The second of the six global goals aims for a 50% reduction of anemia in female of reproductive age by 2015 (WHO 2014b).

TABLE 1 **Classification of anemia in pregnancy according to WHO**

Pregnancy trimester	*Normal (g/dL)*	*Mild (g/dL)*	*Moderate (g/dL)*	*Severe (g/dL)*
1st	≥11	10–10.9	7–9.9	<7
2nd	≥10.5			
3rd	≥11	10–10.9	7–9.9	<7

- Sustainable Development Goals (SDGs); according to the second goal on ending hunger, target 2.2 aims to end all forms of malnutrition by 2030 (UN 2015)
- Under **POSHAN Abhiyaan**, the government targets to decrease the incidence of malnutrition by 2% a year and anemia prevalence by 3% a year.
- Overall, India plans to reduce anemia levels to one-third of what was recorded in the fourth **National Family Health Survey, by 2022.**

Erythropoiesis is the process by which hemoglobin will be synthesized.

Factors required for erythropoiesis:

- Proteins (erythropoietin)
- Minerals (iron)
- *Trace elements:* Zinc, Cobalt, Copper, etc.
- *Vitamins:* Folic acid, Cyanocobalamin (B_{12}), Vitamin C, Pyridoxine (B_6), Riboflavin, Vitamin A, and Vitamin D
- *Hormones:* Androgens & Thryoxine

Anemia due to nutritional deficiency (the commonest type of anemia) happens if the body doesn't absorb enough of nutrients, the factors required for erythropoiesis.

Iron-Deficiency Anemia

Iron deficiency is the most common nutritional deficiency in India.

Sources of Iron

Common sources of heme iron which can be easily absorbed are fish, meat, prawns, etc, non heme iron which needs other micronutrients like Vitamin C are dried fruits like dates, raisins, figs; legumes like beans, peas; green leafy vegetables like spinach, kale, moringa; nuts like almonds, cashew; seeds like pumpkin, sesame, flaxseeds, etc.

Functions and Homeostasis of Iron

- Part of hemoglobin and myoglobin.
- Part of enzymes like cytochromes, catalase, peroxidase.

- Oxygen transport and cellular respiration.
- Cellular immune response and functioning of phagocytes.
- Brain development and function.
- Regulation of body temperature and muscle activity.

New Revelation—Role of Hepcidin Mediated Regulation of Iron Homeostasis (Fig. 1)

- *Anemia of chronic diseases:* Inflammatory stimuli → Increased hepcidin expression by the liver → High levels of hepcidin in the bloodstream → internalization and degradation of the iron exporter ferroportin. → macrophage iron loading, low plasma iron levels → anemia of chronic disease.
- *Normal:* Normal hepcidin levels, in response to iron demand, regulate the level of iron import into plasma, normal transferrin saturation, and normal levels of erythropoiesis.
- *Hemochromatosis (iron overload):* from insufficient hepcidin levels → increased iron import into plasma, high transferrin saturation, and excess iron deposition in the liver. Source: De Domenico, *et al.*

Nutritional and Dietary Causes of Iron Deficiency Anemia

- Reduced intake of enough iron
- Not consuming enough Vit. C
- Having a disease that prevents the body from sufficiently absorbing the nutrients

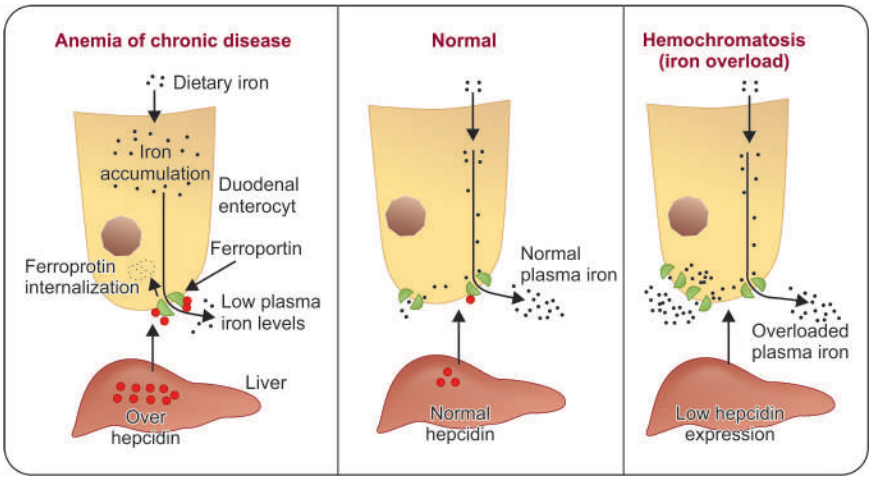


Fig. 1: Mechanism of absorption of iron

Signs and Symptoms Specific to Iron Deficiency Anemia

Syndromes of Plummer – Vinson or Paterson – Kelly (difficulty in swallowing with esophageal webs and atrophic glossitis), gastric mucosal atrophy, stomatitis due to rapid turning over of epithelial cells, spoon shaped nails (koilonychias) and pallor. These changes are due to a decrease of iron-containing enzymes in the GI tract. The restless leg syndrome might be prevalent in pregnancy. Pica, the eating disorder in which there is an appealing desire to lick or eat non-food items such as chalk, soil, ice (pagophagia), or paper is prevalent in pregnant women. Pagophagia (intense desire to eat ice) is specific to iron deficiency and responds quickly to treatment.

Strategies suggested to prevent iron deficiency include:

- Dietary improvement
- Food fortification
- Iron supplementation
- Helminth control

- *Dietary recommendations for better iron intake include:*
  - Consuming tablets at least an hour after a meal (in case of vomiting, nausea or gastritis) for better absorption.
  - Avoiding consumption with coffee, tea, calcium tablets, or milk.

Enhancers of absorption	Inhibitors of absorption
Vitamin C	Oxalate in vegetables
Organic acids – Citrus	Tannin
Sprouted and fermented food	Phosphate egg yolk
Meats and Fishes	Proteins

- *Food fortification:*
  - Several iron fortificants have been used successfully.
  - Rice in Philippines is fortified with iron sulfate mix.
  - Ferrous sulfate has been used in Chile as turnaround time between milling and consumption is less.
  - As our wheat and maize are stored for a longtime, metallic iron has been used in UK, USA, and Sweden and ferrous sulfate in Venezuela.
  - Iron EDTA has been successfully fortified in condiments such as curry powder in South Africa and sugar in Guatemala.

- *Iron supplementation:*
  Iron salts commonly used are:
  - Ferrous sulfate: 20% elemental iron
  - Ferrous fumarate: 33% elemental iron
  - Ferric salts: 18% elemental iron; not preferred over ferrous salts
  - Iron polymaltose complex

- Ferrous aminoate (10% iron)
- Carbonyl iron
- Colloidal ferric hydroxide (50% iron)

A Cochrane systematic study was done to evaluate the efficacy of daily iron alone or along with folic acid or other micronutrients compared with placebo or no iron in pregnant women which displayed a significant reduced risk of maternal anemia, iron deficiency anemia at term. Intermittent supplementation associated with fewer side effects, although the risk of mild anemia near term was increased. Intermittent supplementation has been proposed as a feasible alternative to daily supplementation for those pregnant women who are not anemic and attend adequate antenatal care. WHO recommends once in a week iron and folic acid supplementation (120 mg elemental iron and 2.8 mg folic acid) in non-anemic pregnant women and adolescents. MoHFW recommend iron and folic acid supplementation (100 mg elemental iron and 0.5 mg folic acid) in all females of reproductive age (15–45 years).

In an RCT, various iron supplementations were compared in pregnant women, and found out that ferrous ascorbate and bisglycinate were more effective and better tolerated than ferrous sulfate. The PERFECT trial, a multi-centric RCT, compared ferrous fumarate with carbonyl iron efficacy and tolerability for the treatment of iron deficiency anemia (IDA) in pregnancy, demonstrated a significantly greater incidence of increase in Hb in the patients with ferrous fumarate compared with carbonyl iron. Ferrous fumarate was tolerated well than carbonyl iron as shown by patient global assessment of response to therapy (PGART) score and patient global assessment tolerability to therapy (PGATT) score scales response.

Recommendations by WHO and MoHFW

See **Table 2**.

TABLE 2 **Various iron supplementation regimens according to WHO and MoHFW**

	During	***Pregnancy***	***Postpartum***
	For Prophylaxis	For Treatment	
World Health Organization	60 mg iron + 400 mcg folate till term, daily	120 mg iron + 400 mcg folate till term, daily	60 mg iron and 400 mcg folate – 3 months, daily
Ministry of Health and Family Welfare of India	100 mg iron + 500 mcg folate for 100 days starting, daily after 1st trimester, at 14–16 wks of gestation	Mild anemia–2 IFA tablets/day–100 days Moderate anemia – IM iron therapy + oral folate	100 mg iron + 500 mcg folate – 6 months, daily

New Comer – Iron Sprinkles

Recently, a new approach using sprinkles has also been found effective for treatment of iron deficiency anemia.

The Toronto University has developed a supplement containing micro encapsulated ferrous fumarate in powdered form plus ascorbate which can be sprinkled on to any food item. The supplement is referred to as supplefer sprinkles.

Vitamin C and Anemia

- Bioavailability of food iron strongly depends on presence of enhancers and inhibitors in the diet.
- Presently, there is no satisfactory in vitro method for predicting the bioavailability of iron in a meal.
- Iron absorption varies from 1% to 40%, depending on the presence of enhancers and inhibitors in the meal.
- Therefore, the adequacy—i.e., bioavailability—of iron in usual diets can be altered by altering meal patterns to increase enhancers, decrease inhibitors, or both.
- One of the major enhancer is Vitamin C.

RDA of vitamin C: See **Table 3**.

Common Vitamin C rich foods are: Cabbage (patta gobhi), Drumstick leaves (Saijan patta), Coriander leaves (Dhaniya), Gooseberry (Amla).

Folic acid & B12 deficiency: Folic acid also known as Vitamin B9. Necessary for DNA synthesis. Cooking destroys folic acid.

Sources:
Folic acid: 12 foods rich in folic acid leafy greens, asparagus, broccoli, papaya & oranges, avocado, seeds & nuts, brussels & sprouts, beans, peas & lentils, okra, cauliflower, beets, bell pepper.

B12: Milk, meat, shellfish, supplements, egg, fortified cereals.

Causes: Strict vegetarian, Repeated pregnancy, Chronic diarrhea, malabsorption, and recurrent infections.

RDA of vitamin B12: See **Table 4**.

Symptoms: A sensation of tingling or pins & needles, sore & red tongue, mouth ulcers, muscle weakness, fatigue & lack of energy, visual disturbances, depression, confusion & other problems with concentration, thinking, and memory.

Long-term complications: Infertility which is usually reversible, complications during pregnancy, congenital disorders, nervous system disorders, etc.

TABLE 3 **Tolerable upper intake levels (ULs) for vitamin C according to ICMR**

Age	*Male (mg)*	*Female (mg)*	*Pregnancy (mg)*	*Lactation (mg)*
0–12 months	Not possible to estabish*	Not possible to estabish*		
1–3 years	400	400		
4–8 years	650	650		
9–13 years	1,200	1,200		
14–18 years	1,800	1,800	1,800	1,800
19+ years	2,000	2,000	2,000	2,000

*Formula and food should be the only sources of vitamin C for infants.

TABLE 4 **RDA of vitamin B12 according to ICMR**

Population	*RDA of Vit B12 (mcg)*
14 years and above	2.4
Pregnant women	2.6
Lactating women	0.8

Deficiency disease: Megaloblastic anemia in children & pregnant mothers **(Fig. 2)**.

Treatment: Folic acid 2–5 mg/day, RDA: 500 mcg/day for pregnant mother.

Prevention of Vit B12 deficiency: In prolonged medication use such as H2 blockers or PPI- screening to be considered (if >12 month of use), metformin (for >4 month of use). RDA to be maintained.

Vitamin B12 supplements: IM injections of cyanocobalamin or oral vitamin B12 therapy.

- Approximately 10% of the standard injectable dose of 1 mg is absorbed, which allows for rapid replacement in patients with severe deficiency.
- British Society for Hematology—recommends injections three times per week for 2 weeks in patients without neurologic deficits.
- If neurologic deficits, injections should be given every other day for up to 3 weeks or until no further improvement is noted.

Vitamin D deficiency: 60–90% Indians have vitamin D deficiency. Approx. 50% of those have anemia **(Fig. 3)**.

Sources of Vitamin D: Vitamin D is synthesized in the skin by UV light exposure or can be obtained by consumption of fish oil, fatty fish, oysters, butter, mushrooms, beef, liver, cheese, egg yolk. Sunlight exposure is

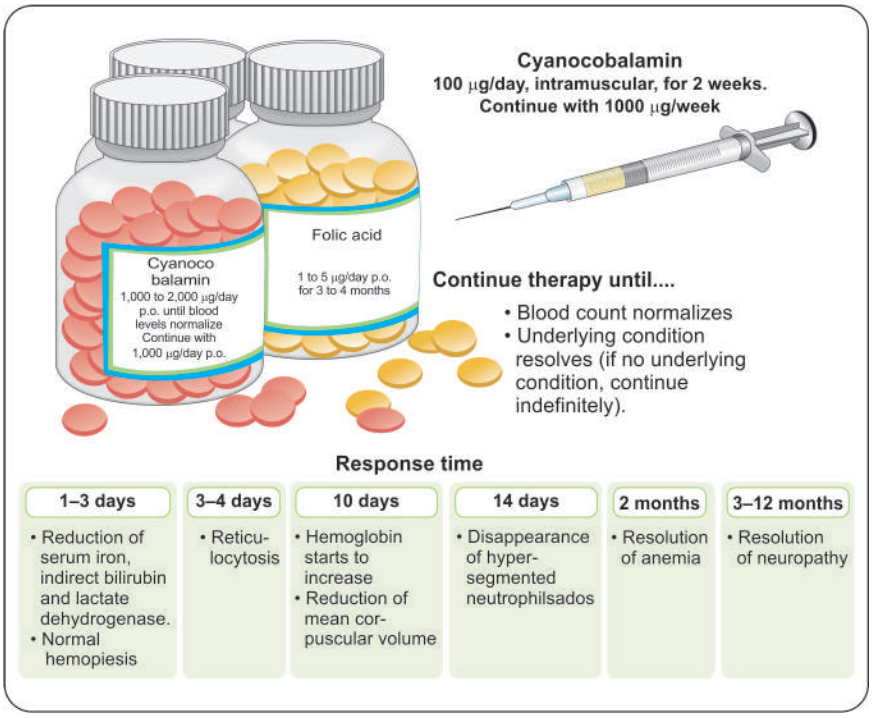


Fig. 2: Pharmacological management of megaloblastic anemia

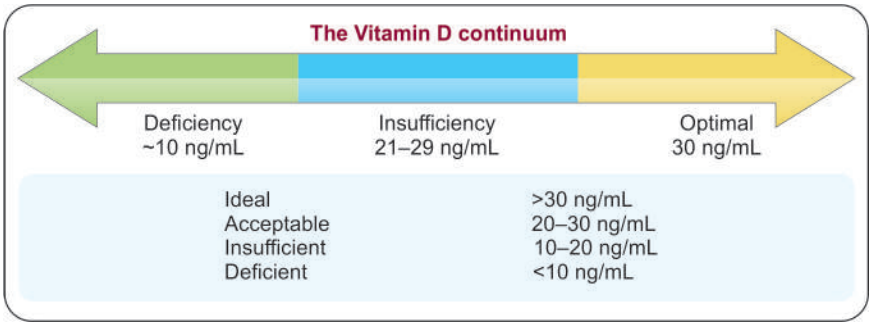
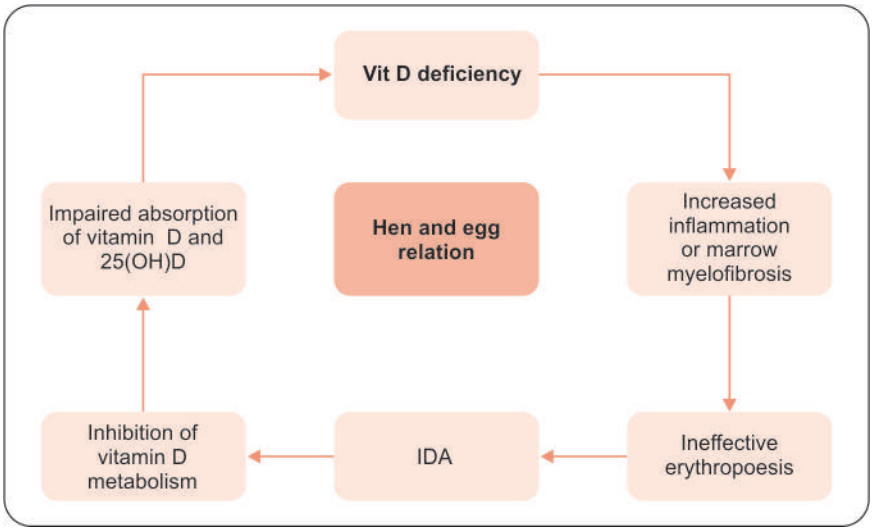


Fig. 3: The vitamin D continum or spectrum

influenced by skin color, latitude, season, lifestyle, and cultural practice, 10–15 mins sunshine, thrice a week is enough to produce the vit D needed for the body **(Flowchart 1)**.

Treatment: Vitamin D RDA is 600 IU. At booking all pregnant women are offered vitamin D testing in early pregnancy. Levels < 75 nmol/L – vitamin D supplementation of 1000 IU combined with 1 gm calcium per day.

Flowchart 1: Mechanism of absorption of vitamin D



Zinc Deficiency

Zinc is the cofactor of several enzymes and plays a role in iron metabolism, so zinc deficiency is associated with IDA.

Zinc is a trace element that functions in several processes in the body, and zinc deficiency aggravates IDA symptoms. Measurement of zinc levels and supplementation if necessary should be considered for IDA patients.

Vitamin A and Anemia

Vitamin A is also involved in the pathogenesis of anemia through various mechanisms, such as the increase of growth and differentiation of erythrocyte progenitor cells, enhancement of immunity to infection and mobilizing the iron stores from tissues.

In a study by suhamo et al., a combined iron and vitamin A supplement for pregnant women in Indonesia was needed where both deficiencies were common.

Anemia in Protein Deficiency

Decreased dietary intake of *protein* may lead to mild to moderate anemia. Anemia caused by protein deficiency is also called "*hypoproliferative anemia*". Mainly seen in decreased intake vegans, vegetarians, elderly, endurance athletes, anorexia nervosa, chronic liver disease, etc. **(Fig. 4 and Flowchart 2)**.

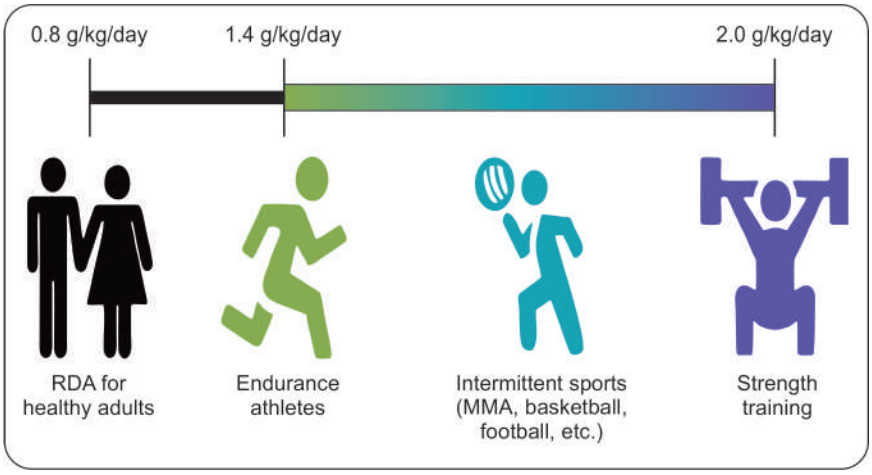


Fig. 4: RDA of protein

Flowchart 2: Mechanism of action of protien in RBC production

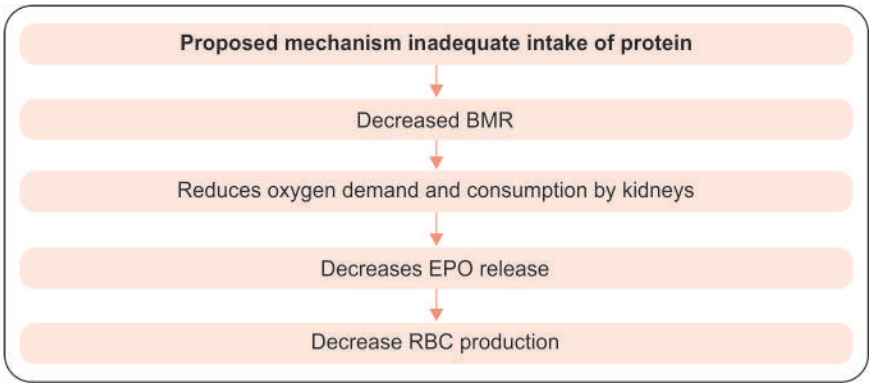


TABLE 5 **Summary of recommended intakes for other minerals and trace elements**

Minerals/trace element	*Recommended intake*
Phosphorous	1000 mg/day
Sodium	2000 mg/day
Potassium	3500 mg/day
Copper	2 mg/day
Manganese	4 mg/day
Chromium	50 µg/day
Selenium	40 µg/day

TABLE 6 **ICMR guidelines-2020, Summary of year for Indians-2020**

Age group	Category of work	Body weight (kg)	Energy (**) (kcal/d)	Fats/oils (visible) (#) (g/d)	Protein (g/d)	CHO (g/d)	Calcium (mg/d)	Magnesium (mg/d)	Iron (mg/d)	Zinc (mg/d)	Iodine (g/day)	Thiamine (mg/d)	Riboflavin (mg/d)	Niacin (mg/d)	Vitamin B6 (mg/d)	Folate (µg/d)	Vitamin B12 (µg/d)	Vitamin C (mg/d)	Vitamin A (µg/d)	Vitamin D (IU/d)
Men	Sedentary		2110	25								1.2	1.6	12	1.6					
	Modrate	65	2710	30	42.9	100	800	320	11	14.0	95	1.5	2.1	15	2.1	250	2	65	460	400
	Heavy		3470	40								1.9	2.7	19	2.6					
Women	Sedentary		1660	20								1.1	1.6	9	1.6					
	Modrate	55	2130	25	36.3	100	800	270	15	11.0	95	1.4	2.0	12	1.6	180	2	55	390	400
	Heavy		2720	30								1.8	2.6	15	2.1					
	Pregnant woman	55 + 10	+350	30	+7.6 (2nd trimester) + 17.6 (3rd trimester)	135	800	320	32	12.0	180	1.6	2.3	+2	1.9	480	+0.2	+10	406	400
	Lactation 0–6 m		+600	30	+13.6	155	1000	270	16	12.0	200	1.7	2.5	+4	+0.22	280	+0.8	+40	720	400
	7–12 m		+520		+13.6	155						1.7	2.4	+4	+0.16	280				
Infants	0–6 m*	5.8	550	—	6.7	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	6–12 m	8.5	670	25	8.8	—	—	—	2	2.0	130	—	—	—	0.5	71	1	—	170	—
Children	1–3 y	11.7	1010	25	9.2	100	400	111	6	2.5	65	0.6	0.8	6	0.8	90	1	22	180	
	4–6 y	18.3	1360	25	12.8	100	450	131	8	3.7	80	0.8	1.1	8	1.0	111	1	27	240	400
	7–9 y	25.3	1700	30	19.0	100	500	178	10	4.9	80	1.0	1.3	10	1.3	142	2	36	290	
Boys	10–12 y	34.9	2220	35	26.2	100	650	223	12	7.0	100	1.3	1.7	12	1.7	180	2	45	360	400
Girls	10–12 y	36.4	2060	45	26.6	100	650	214	16	7.1	100	1.2	1.6	12	1.6	186	2	44	370	400
Boys	13–15 y	50.5	2860	50	36.4	100	800	294	15	11.9	100	1.6	2.2	16	2.2	238	2	60	430	400
Girls	13–15 y	49.6	2400	35	34.7	100	800	270	17	10.7	100	1.3	1.9	13	1.8	204	2	55	420	400
Boys	16–18 y	64.6	3320	40	45.1	100	850	338	18	14.7	100	1.9	2.5	19	2.5	286	2	69	480	400
Girls	16–18 y	55.7	2500	35	37.3	100	850	279	18	11.8	100	1.4	1.9	14	1.9	223	2	57	400	400

*: AI; **: There is no RDA for energy. The EAR is equivalent to Estimated Energy Requirement (EER); #: Visible fat requirement is in proportion to EER

TABLE 7 **Tolerance upper limit (TUL) for nutrients**

Age group	*Category of work*	*Protein (PE ratio)*	*Calcium (mg/d)*	*Magnesium (mg/d)*	*Iron (mg/d)*	*Zinc (mg/d)*	*Iodine (g/day)*	*Niacin (mg/d)*	*Vitamin B6 (mg/d)*	*Folate (µg/d)*	*Vitamin C (mg/d)*	*Vitamin A (µg/d)*	*Vitamin D (IU/d)*
Men	Sedentary	<40%	2500	350	45	40	1100	35	100	1000	2000	3000	4000
	Modrate												
	Heavy												
Women	Sedentary	<40%	2500	350	45	40	1100			1000	2000	3000	
	Modrate												
	Heavy												
	Pregnant woman	<30%	2500	350	45	40	1100	—	—	1000	2000	3000	4000
	Lactation 0–6 m 7–12 m	<40%	2500	350	45	40	1100	—	—	1000	2000	3000	4000
Infants	0–6 m	<15%	—	—	40	4	—	—	—	—	—	600[$]	1000
	6–12 m	<15%	—	—	40	5	—	—	—	—	—	600[$]	1500
Children	1–3 y 4–6 y 7–9 y	<15% <15% <15%	1500 2500 2500	65 110 100	40 40 40	7 12 12	200 300 400	—	—	— — 300	350 550 800	600[$] 600[$] 600[$]	2500 3000 3000
Boys	10–12 y	<15%	3000	350	40	23	600	—	—	600–800 (9–17 y)	1050	1700	4000
Girls	10–12 y	<15%	3000	350	40	23	600	—	—	—	1300	1700	4000
Boys	13–15 y	<15%	3000	350	45	34	900	—	—	—	1550	2800	4000
Girls	13–15 y	<15%	3000	350	45	34	900	—	—	—	1800	2800	4000
Boys	16–18 y	55.4	3000	350	45	34	1100	—	—	—	1950	2800	4000
Girls	16–18 y	55.4	3000	350	45	34	1100	—	—	—	2000	2800	4000

$: adopted from IOM

Protein rich foods: Milk, chicken, nuts, egg, dal, oilseeds.

Protein deficiency management: Find and treat underlying cause

- Protein rich diet a/c age
- Protein supplements-1-2 g of protein and 30-60 cal/kg to 100 cal/kg
- parenteral amino acids can be used in critically ill patients to stimulate whole-body protein accretion.

Copper: Heme synthesis is interfered in copper deficiency. Clinical deficiency is very rare. Between 0.5–5 mg of copper salts/day may be given therapeutically; prophylactic dose is 0.1 mg/day. It is present in some hematinic combinations.

Summary of recommended intakes for other minerals and trace elements: See **Table 5**.

Riboflavin: Hypoproliferative anemia occurs in deficiency of riboflavin which is generally a part of multiple deficiencies in calorie protein malnutrition.

In the absence of specific deficiency, use of riboflavin in anemia is of no value. Summarized RDA for energy in **Tables 6 and 7**.

Conclusion

Nutritional deficiency anemia is a common problem. It can occur when the body is not absorbing enough nutrients from diet. The problem may be that the diet is insufficient or that an underlying medical condition or treatment interferes with the body's ability to absorb these nutrients. Having a healthy and varied diet can usually provide enough nutrients to prevent anemia.

Bibilograpghy

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Chapter 10

Medical Nutritional Therapy in Management of Gestational Diabetes Mellitus—A More Practical Approach

Hema Divakar, Sheetal Joshi

Introduction

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy.[1] Gestational diabetes may be result of insulin resistance due to pregnancy hormones, which is not adequately compensated for by the pancreatic β-cells through increased proliferation and insulin secretion. The pathogenesis of GDM is unknown, but considering increased number of gestational diabetes cases the factors can be genetic or nongenetic factors, including maternal age, obesity, diet, and lifestyle.[2] The prevalence of gestational diabetes has been reported from 3.8% to 17.9% in different parts of India. It is difficult to predict any uniform prevalence levels of GDM in India, because of wide differences in living conditions, socioeconomic levels, and dietary habits.[3] Since India is focusing on universal screening of all pregnant women for GDM, and given the recent changes in diagnostic criteria, there is going to be a substantial increase in the numbers of pregnant women who shall be diagnosed with GDM. Once diagnosed with GDM, all of them become candidates for management of the condition. *It is seen that almost 80–90% of them can be managed with Medical Nutrition Therapy (MNT). All the recent international workshop-conferences on GDM have also recognized MNT as the cornerstone of therapy for women with GDM.*[4]

What Is Medical Nutrition Therapy?

MNT for GDM has been defined as a *"carbohydrate-controlled meal plan"* that promotes:

- adequate nutrition,
- appropriate weight gain,
- normoglycemia,
- ensures the absence of ketosis.[5]

MNT plays an important role in the management of GDM, and accordingly, it has a significant impact on women and newborns. The primary objective of

MNT is to ensure adequate fetus growth while maintaining euglycemia and avoiding ketones.[6]

According to *National Guidelines for Diagnosis & Management of Gestational Diabetes Mellitus*[6]

All pregnant women with GDM should get MNT as soon as diagnosis is made.

Indian guidelines do outline particular recommendation about MNT in GDM in addition to general guidelines on diagnosis and treatment of GDM. Latest DIPSI guidelines have also mentioned the amounts of calories and its distribution.

Principles laid out by some of the recommended *Guidelines across the world* from the UK, ADA, ADIP, NICE, DDG-DGGG are similar and as follows:

- Diabetes UK, the diabetes association in the United Kingdom, only gives one piece of general advice for GDM: offering individualized nutritional education and providing access to a multidisciplinary team.[7]
- The ADIPS and ADA encourage individualizing healthy food plans to each patient's culture, weight gain, and physical activity and modifying these food plans during pregnancy if necessary.
- The ADIPS and ADA support training patients in CHO counting.
- NICE guidelines specify some healthy diet recommendations such as to increasing the intake of fruits and vegetables, not eating for two, and avoiding drinking full fat milk.
- The DDG-DGGG guidelines recommend explaining a diet using German units to measure CHO in diabetes.

A Practical Approach

It's often observed that MNT can be significantly used to address the GDM issues. Some of the practical approaches have been highlighted here.

Nutritional Assessment – Think Nutrition First

Nutritional assessment is the first step in management of GDM. FIGO also recommends a nutritional checklist for the same[8] (checklist can be downloaded from www.figo.org) **(Fig. 1)**. This is required to create a customized diet plan with balanced calorie distribution and its implementation. To arrive at this customized diet, the anthropometric measurements like Age, Height, Weight, and BMI have to be recorded.

Another important parameter to be taken into account is the number of weeks into the pregnancy since the onset of various pregnancy hormones has an impact on blood glucose values. Of course, the diet plan also needs to take care of the cultural background, special preferences in eating beliefs like vegetarian, non-vegetarian, vegan, etc., likes & dislikes during pregnancy.

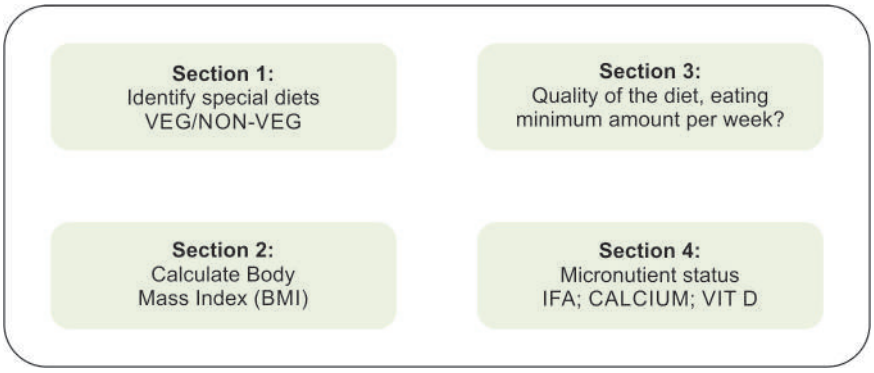

Fig. 1: Break down of the FIGO nutrition checklist

The 24-hour dietary recall method and checking biochemical parameters will help to understand the dietary needs and nutritional deficiencies. Last but not the least the medications and supplements have to be considered to make a fool-proof eating plan.

Calorie and Macronutrient Distribution

Calculation of calories and macronutrients is a crucial part in creating the practical approach toward planning a ideal diet.

Calories

The calories required are calculated based on BMI. The caloric requirement of women with GDM at IBW is 30 kcal/kg/day, overweight 24 kcal/Kg/day, obese 12–15 kcal/kg/day.

Considering the requirement the diet plans vary from 1,800 kcal/day to 2,400 kcal/day, ADA recommends the distribution of calories to be carbohydrates 50% – minimum 175 gm 10% breakfast, 30% lunch, 30% dinner, 30% snacks. With low GI and low GL. Protein 20% and 30 % from fats <7% saturated fats. Include omega 3 fatty acids.[9]

How you can plan a meal based on calories?

Based on BMI, lets presume the requirement is 1,800 kcal. Simple method is

*400 kcal/per meal*3 = 1,200 kcal

and

*200 kcal/per snack*3 = 600 kcal

In GDM, postprandial sugars are high. So, split 400 kcal/2 = 200 kcal.

Plan 8 meals of 200 kcal, with similar dietary composition. Reassess, usually post breakfast are high. Try decreasing calories, changing carbohydrate type.

Don't give available carbohydrates in first meal definitely, and less amount in next meal. A mixed meal consisting of carbohydrate, protein, fat, and fiber eaten together results in slow blood sugar rise.

Carbohydrates

Carbohydrate foods are essential for a healthy diet of mother and baby. Once digested, carbohydrate foods are broken down to glucose. Hence, carbohydrate is the primary nutrient that affects Postprandial blood glucose.[9] But there should not be too much carbohydrate restriction as carbohydrates are not only energy giving foods but also mood enhancing foods during pregnancy; according to ADA it should be about 45–50% of total daily energy intake or 175 gm for pregnant woman.

To avoid carbohydrate loading the carbohydrates should be distributed equally throughout the day into three-moderate size meals and three to four snacks.[10] The type, amount, and frequency of carbohydrate intake has a major influence on blood sugar readings. As shown in **Figure 2** the time taken for food to get converted in blood glucose depends on type of nutrients.

Carbohydrate counting is one of the good methods to keep control over intake of carbohydrates. It involves counting the number of carbohydrates.

How do you count carbohydrates?

Carbohydrates are measured in grams and may be referred to in grams, exchanges, servings, or carb choices. *A food that contains 15 gm of carbs is called 1 carb exchange.*

1 Exchange = 1 Choice = 1 Carb = 1 Portion = 1 CP (Carb Portion) = 1 CU (Carb Unit) = 15 gm carbohydrate **(Fig. 3)**

This method helps:

- The patient to manage portion size
- The consumption of carbohydrate reduces
- Easy to make a meal plan
- Gets to eat variety of foods

Foods sources of carbohydrate include **(Fig. 2)***:*

- Cereals (wheat, bajra, ragi, corn rice, etc.) and its products (suji, refined flour, breads, pasta, noodles, etc.),
- Pulses, legumes, beans (green gram, Bengal gram, black gram, etc.),
- All vegetables including starchy vegetables (potato, sweet potato, corn tapioca, etc.)
- Fruits, sweets, juices, etc.
- Milk, yogurt, cottage cheese.

  Any one serving of any carbohydrates is approximately = 1 exchange.

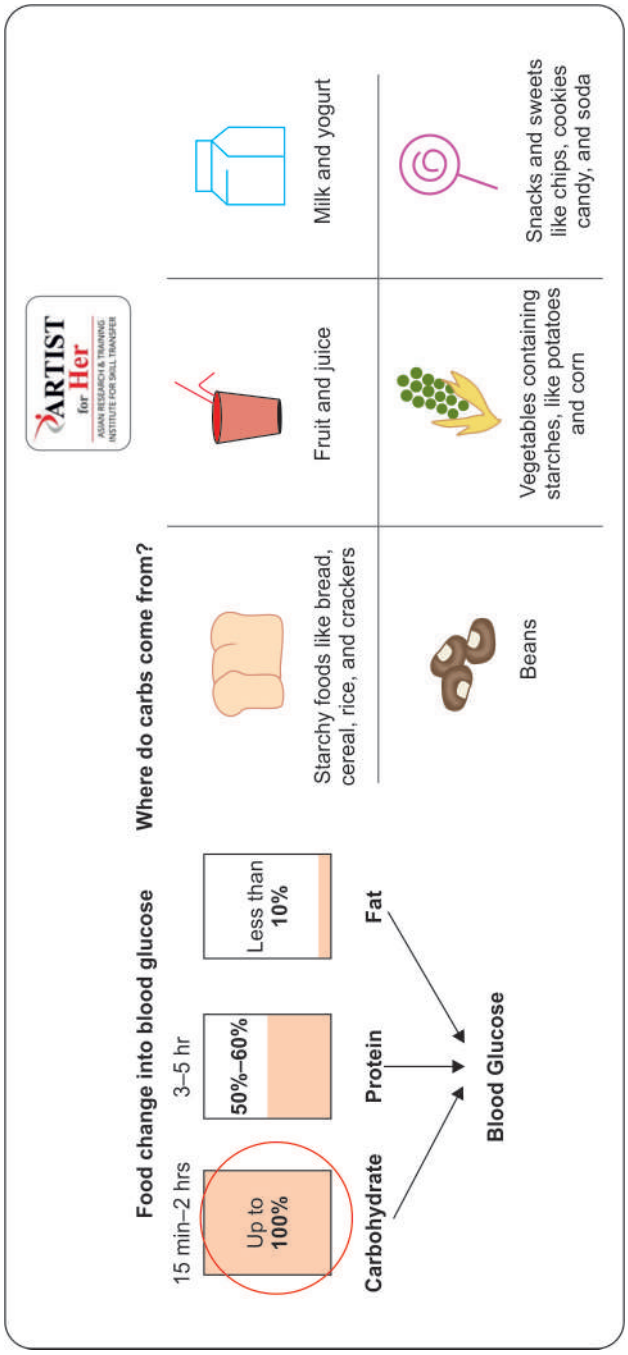

Fig. 2: Why type of food matters?

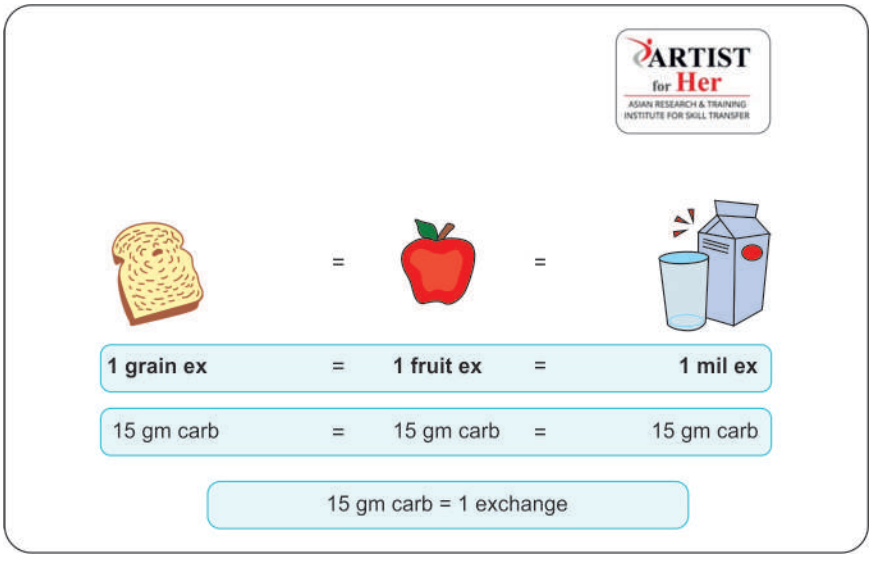

Fig. 3: What is carbohydrate counting?

How do you count number of exchanges required?

Example: 1,800 kcal/day diet = 15 exchanges.

Meal	*Early morning*	*Breakfast*	*Mid-morning*	*Lunch*	*Evening snack*	*Dinner*	*Bedtime*
Carbohydrate allowance	7.5 gms (½ Ex)	45 gms (3 Ex)	15 gms (1 Ex)	60 gms (4 Ex)	30 gms (2 Ex)	60 gms (4 Ex)	7.5 gms (1/2 Ex)

How to reduce carbohydrates?

- Reduce the serving size of cereals/grains. Increase pulses, legumes, millets, and non-starchy vegetables.
- Avoid all packaged food, bakery products, refined foods.
- Consume whole fruit instead of juice.
- Choose unpolished variety of grains with fiber.
- For sweet craving a small amount of dry fruits are better option than any biscuits or chocolates.

Proteins

Protein intake is very important during pregnancy to compensate the increase in protein synthesis, maintaining maternal tissues and fetal growth. The necessity of protein during gestation and lactation is not different in women with or without diabetes. Apart from fetal growth proteins and amino acids in the diet are significant regulators of glucose homeostasis, and a high-

protein diet contributes to insulin resistance and increases gluconeogenesis. which helps to control postprandial glucose spike. It also gives satiety which can decrease calorie intake.[9]

Protein content in the ADA diet and euglycemic diet makes up 20% of the total daily caloric intake. Protein RDA is 1 g/kg/day for normal women. In the 3rd trimester of pregnancy (+23 g/day) (ICMR 2010), Protein requirement in pregnancy is increased (+23 g/day) to allow for fetal growth. At least three serving of protein foods are required every day to meet increased demand.

Most of the Indian pregnant women do not enjoy proteins, especially vegetarians because of the smell, which they cannot tolerate. They complain of bloating and gas with intake of dals & pulses. Women who intake meat are discouraged from consuming it once they become pregnant since eating such food are considered as "hot" food. Constipation is another major issue. Solution is to find recipes and process of cooking proteins by soaking, grinding, fermenting, sprouting, and cooking it well.

How to increase protein intake?

Firstly, by understanding the sources of proteins one can easily ensure inclusion of them in every meal.

- Add vegetables, peanuts, green peas in the breakfast.
- Rotate various pulses and millets.
- Combine legumes/pulses/grams along with vegetables for a wholesome curry and in this way improve the quality of protein. Soya chunks and tofu can also be used.
- Garnish curries/salads with roasted peanut powder, sesame seeds (til).
- Indulge in fistful of nuts and seeds as mid-morning or evening snacks.
- Include dairy products, milk, yogurt, or cottage cheese (paneer).
- If allowed, eggs, fish, chicken, or mushrooms can also be consumed.
- Mix soya flour (20%), besan (channa dal) (20%), flaxseeds powder to wheat/jowar/ragi flours (60%) to make chapatti/roti as shown in **Figure 4**.

Fats

About 30% of the total calories are recommended from fat sources. Consumption of oil, ghee, butter all included should be limited to 0.5 kg/month/person. A blend of two or more vegetable oils should be used in daily cooking. Diet should be low in saturated fats and Limit trans fats – baked products, cookies, chips. Adequate intake of EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid) of 300 mg/day EPA reduces inflammation, dilates blood vessels, and reduces blood clotting DHA is a major structural component of phospholipids in cell membranes in central nervous system. Encourage monounsaturated fats.[11]

Fig. 4: High protein roti

How to include good fats?

The diet should have fats from monounsaturated fatty acid, polyunsaturated fatty acids, and saturated fats (<7%). This can be achieved by choosing different types of oils on rotation (regional, local, traditional filtered cold pressed oils) or using different type of fats for different recipes as it was done traditionally. Mid morning or evening snacks can be seeds and nuts. They can also be roasted and crushed to garnish salads. To remove the phytic acid which stops the absorption of iron and zinc, roasting or soaking of nuts and seeds is a very important process. DHA and EPA can be got from fishes, nuts, and flaxseeds.

Understanding the type of fats and its sources help in including them in the diet plan.

Monounsaturated fat: good sources include: Olive, canola, peanut, and sesame oils, Avocados, Nuts (almonds, peanuts, macadamia, hazelnuts, pecans, cashews), Peanut butter.

Polyunsaturated fat: good sources include: Sunflower, sesame, and pumpkin seeds, Flaxseed, Walnuts, Fatty fish (salmon, tuna, mackerel, herring, trout, sardines) and fish oil, Soybean, safflower oil, Soymilk, Tofu.

Saturated fats good sources include: Whole-fat dairy products (milk, cream, cheese, ghee, butter), Tropical oils such as coconut and palm oil.

Fiber

There are evidence which suggests that high-fiber diets, especially of the soluble variety, and soluble fiber supplements may offer some improvement in carbohydrate metabolism, also including fiber in the diet aids in improving satiety, preventing constipation which is commonly observed in pregnancy.[9] Constipation during pregnancy is because of high levels of the hormone progesterone which slow down the muscle contractions that normally move food through your system. Add to that the extra iron given from prenatal vitamin increases constipation. An intake of up to 25–30 gm of fiber per day or 25 g/1,000 kcal of food intake appears beneficial as fiber slows down the gastric emptying and delays release of sugar.

How to increase fiber?

The inclusion of whole fruits, vegetables, and sprouts, whole grains, steel cut oats, nuts, seeds, millets will help improving fiber in the food. Include as many vegetables and course rava, brown rice flakes, broken wheat, millet dosa for breakfast. The whole grains and unpolished grains are good choice as shown in **Figure 5**.

Fig. 5: Vegetables and cereals with husk to increase fibre

Role of Other Nutrients

- Calcium requirements increase in pregnancy. Calcium rich foods such as low fat cow's milk, curd, cheese, green leafy vegetables, millets like ragi, sesame seeds, amaranth seeds should be included.
- Increased iron requirements can be met by including (ragi), rajma, green leafy vegetables especially drumstick leaves, nuts (soaked) and seeds, egg, fish, including Vitamin C for better absorption.
- Myo dichiro inositol and Vitamin D supplements are shown beneficial in management of GDM.

Probiotics: Numerous studies show that probiotics can reduce the incidence of GDM. Probiotic use in pregnancy could significantly reduce the fasting glucose levels. Probiotic food supplements are available from many sources but effectiveness is dependent on various factors like temperature, anaerobic storage conditions, the initial dose of the strain and its quality.[12]

How to include probiotics?

Easily available pre- and probiotic is from 'Raita' which is a combination of vegetable and yogurt. Fermented foods, traditional pickles, and buttermilk consumption can also be beneficial.

Splitting the Breakfast

It has been observed that the postprandial blood glucose is high during the breakfast. The morning cortisol surge (Dawn Phenomenon) causes the release of glucose from stored sources and hepatic gluconeogenesis creating high blood glucose levels. Therefore, a decreased carbohydrate load is desirable in the breakfast meal. A better approach is to split the single

meal of breakfast into two low carbohydrate meals. Each portion should be consumed with a 2-hour gap in between. This prevents the undue peak in plasma glucose levels after ingestion of the total quantity of breakfast at one time and brings down the postprandial plasma glucose by 20–30 mg/dL.[13]

How to split breakfast?

Splitting the breakfast can be done by giving two carbohydrate exchange in meal 1. after 1 hour blood glucose to be checked and than another two exchange of carbohydrates can be taken. Protein source must be consumed with every meal. Some studies have also shown good control over blood glucose by having similar approach of splitting the other two major meals namely lunch and dinner .

Frequency and Meal Timings

Mealtimes and frequency are very important in management of GDM. Based on the time required for a particular nutrient to get digested and absorbed, the diet should be planned. Include complex carbohydrates every 2 hours as it releases sugars from 15 minutes to 2 hours for digestion. The proteins should be in three main meals as it takes 3 hours to 5 hours for absorption and releases sugars slowly. A bed time snack is important to prevent accelerated starvation in ketosis overnight.

Counseling a GDM Woman

Finally, compliance of the diet plan is always achieved by good counseling. The patient should be made aware of gestational diabetes, its management and consequences. Re-enforcing on some basic important points gives good results **(Fig. 6)**.

- Reduce grain size in 3 main meals.
  No going beyond 2 numbers. For example: 2 idlis, 2 dosa, 2 rotis/chapattis, etc.
  No going beyond 1 medium bowl size of cereals which makes up for 2–3 serving of carbohydrates. For example: A medium bowl of rice, upma, poha, etc.
- Protein source in each meal. For example: Paneer, soyabeans, dals, lentils, legumes, sprouts, boiled groundnut, nuts, seeds, eggs, chicken, fish, milk, etc.
- Adhere to frequency & time of meals. For example: 3 smalls meals, 3–4 snacks, fixed time for all the meals.
- Avoid processed food like bakery items, packaged food and juice and instead reach out for snacks like roasted channa, nuts, seeds, puffed

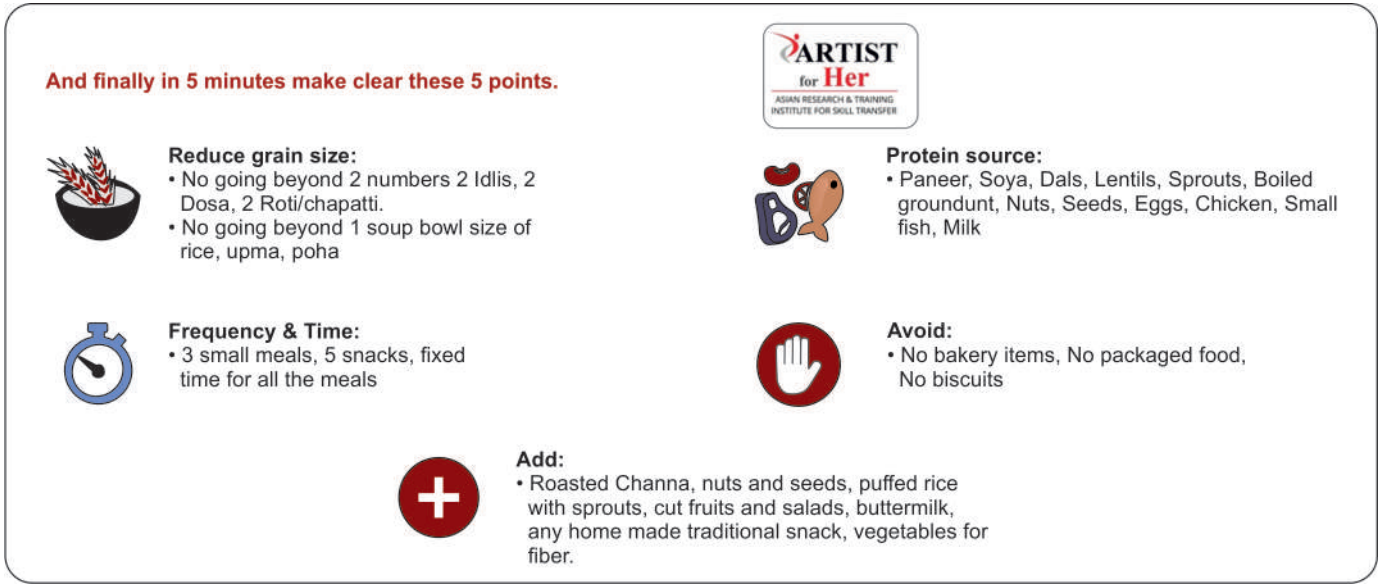

Fig. 6: Five points five minutes GDM diet counseling

rice with sprouts, fresh cut fruits or salads, buttermilk, any homemade traditional snacks, or vegetables with hummus.

- Regular blood glucose monitoring is very important.
- The advice is incomplete without asking her to do simple walks after each meal and pregnancy yoga and exercises under guidance.

Conclusion

Medical nutrition therapy remains the cornerstone of treatment for GDM. It is seen 80–90% can be managed by MNT alone. The diet plan made considering proper distribution of calories and the nutrients can control the blood glucose levels. Including complex carbohydrates, proteins, fats from nuts and seeds, probiotics, micronutrient supplements, splitting the breakfast are the key factors on MNT. Proper counseling a GDM patient with carbohydrate counting, type of nutrients, and mealtimes will surely help in crossing the important phase of pregnancy.

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Chapter 12

Nutrition during Lactation—Eat Right, Baby Bright!

Manpreet Kaur Tehalia, Jyothi GS

Introduction

In order to promote and achieve optimal infant health and development, WHO recommends exclusive breastfeeding for the first 6 months of life.[1] Lactation is a period of mixed feelings for the new mother. There are the fears and anxieties of a new baby in the house, especially for the first timer. The sleepless nights and stolen naps, the fretful baby, the nappies, diapers and washcloths, the burping and the barfing and over all that the anxiety of the care givers at home, with their well-meaning advice, mild reprimands and the milk increasing tips and tricks for "the-best-breastfeeding" makes this a stressful phase in woman's life. The mother must sift through all the information, discard the myths, and simplify her own care routine in order to maintain her own health in those early days and months after childbirth. So, here is a crisp go-to guide for the doctors to dispel the doubts and queries regarding nutrition in lactation and reinforce the facts for their patients.

What Should Lactating Mothers Eat?

Composition of human milk **(Table 1)** depends on three factors:

- Endogenous biosynthesis in the mammary glands.
- Release of fatty acids from tissue deposits laid down during pregnancy.
- *Current diet of the breastfeeding mother* **(Table 2)**.

It is important to emphasize to the mother and her care givers to make her health a priority for the health of the baby.

General Advice[2]

- Choose a variety of foods to build up immunity and pass on the benefits to the baby **(Table 3)**.
- Include foods from all classes **(Table 4)**—Fruits, vegetables, whole grains, dairy, lentils **(Fig. 1)**.
- Avoid certain foods **(Table 5)**.
- Total energy intake—500 kcal MORE than she needed before pregnancy.
- Moderate exercise lifestyle—2200 kcal/day.[2]

TABLE 1 **Constituents of the human milk**[1]

Classes of the constituents in human milk	*Formula milk/cow's milk*	*Classes of constituents in human milk*	*Formula milk/cow's milk*
Proteins & nonprotein compounds		***Carbohydrates***	
Proteins	Yes. Not same quality or bioavailability as human milk	Lactose	Yes
Casein	Yes. Higher amounts, so formula milk more difficult to digest	Oligosaccharides	Yes. Structurally and functionally different
α-Lactalbumin	Yes	Bifidus factor	No
β-Lactalbumin	No	Glycopeptides	
Secretory IgA and other immunoglobulins	No	Lipids	Yes but structurally and functionally different
Lysozymes	No	Triglycerides	″
Enzymes	Yes. Not the same quality/ bioavailability/appropriate amount	Fatty acids	″
Hormones	Same as above	Phospholipids	″
Growth factors	IGF-1	Sterols & hydrocarbons	″
Nonprotein nitrogen compounds	Yes. Not the same quality/ bioavailability/appropriate amount	Fat soluble vitamins	″
		Carotene	″

TABLE 2 **How do the nutrients obtained directly or indirectly from mother's nutrition help the baby?**

***Secretory IgA antibodies commonly found in human milk protective against*[3]**	
Enteric pathogens	***Respiratory pathogens***
Bacteria, Toxins, Virulence Factors	***Bacteria***
Clostridium difficile E. coli Klebsiella pneumoniae Salmonella species Shigella species Vibrio cholerae Parasites Giardia lamblia Viruses Polio virus Rota virus	H. influenzae Streptococcus pneumoniae Virus Influenza viruses Respiratory syncytial virus Fungi Candida albicans Food proteins Cow's milk Soy

Major milk constituent class	***Constituent***	***Function***
Carbohydrates	Lactose (7 g/100 mL) (Disaccharide)	Major source of energy for baby Helps in linear & somatic growth
	HMOs[4] (human milk oligosaccharides)	• Limits the microbe virulence by binding to the receptors present on the cell surface. It further inhibits attachment of pathogenic microbes by allowing specific attachment of Bifidobacterium species to the intestinal mucosa. • The critical modulation of the baby's immune system is allowed by the Bifidum which attaches itself to the dendritic cells. This interaction upregulates the inflammatory cytokine system-IL-0, IL-1. • This has an important effect on the incidence of adult diseases like Intrinsic bowel disease, asthma, rheumatoid arthritis, and perhaps cardiovascular diseases.
Proteins		Provide- • All essential amino acids • Necessary for protein synthesis for baby's growth • Protection from microbes • Help in digestion through enzymes • Development of the GIT • Carriers of other nutrients

Contd...

Contd...

Major milk constituent class	***Constituent***	***Function***
	Lactoferrin[5]	• Iron binding glycoprotein • Free iron in the form of lactoferrin competes with bacteria that need free iron, hence disrupt the growth & multiplication of these bacteria • Release Lipopolysaccharides from bacterial walls and cause their destruction • Binding of iron in the breast milk increases the bioavailability of iron for the baby • Contributes to better growth, health, and development of the baby and later health outcomes
Lipids		• Major source of energy for baby (50–60%)
	Cholesterol	• Helps in sterol metabolism in the baby • May DECREASE the cholesterol levels in later life
	LC-PUFAs-DHA & AA- (Long Chain-Poly Unsaturated Fatty Acids - Docosahexaenoic fatty acid, Arachidonic Acid)	• Improve cognitive development of the baby • Visual development • Immune development • Motor development • Decrease incidence of asthma, allergies, childhood inflammation and obesity rates[6]
	TAGs[5] Triglycerides	• Improved absorption of fat from baby's gut • Increased absorption of Calcium
Phospholipids	Sphingomyelin[6]	• Antitumor activity • May influence Cholesterol metabolism • Anti-infective activity
Maternal Leukocytes		• *Immunoglobulins* against infection • *Plasma cells* which migrate from the mucosa of the maternal breast alveolar cells • Form *Macrophages*
Vitamins[7]		• *A, B1, B2, B5*—Maintain vision • *D*—Protect cell membranes in eye and lungs • *K*-Production of clotting factors • *C*-Antioxidant, healing, supporting Immune system, absorption of Iron • *B1, B5, B6, B12*—Healthy Brain development • *B1, B2, B5*—Conversion of milk nutrients to energy

TABLE 3 **Does maternal diet affect the concentration of any nutrients in maternal milk?**[7]

Nutrient	*Infant reliance on breastmilk*	*Affected by maternal status*	*Affected by maternal diet*	*Affected by maternal supplementation*	*Maternal factors affecting breastmilk concentrations*
Carbohydrates	Yes	No	-	Not applicable	BMI (-), Milk volume (+), preterm delivery (-)
Proteins	Yes	Yes	Amino acid concentration varies by maternal intake	Not applicable	Milk volume (-)
Fats	Yes	Yes	Fatty acid composition varies by intake, Quality of FATS taken by mother vary FA type	Not applicable	% LBW (+), Milk volume (-)
Vitamins					
B1, B2, B6, B12, Folate, C, Choline	Yes	**No**—B1 **Yes**—B2, B12, Folate, C, Choline **Maybe**—B2	**No**—Folate **Yes**—B1, B2, B6, B12, Choline **Maybe**—C	**No**—Folate **Yes**—B1, B2, B6, B12 Choline **Maybe**—B12, C	**B12**—Vegetarianism **Folate**—MTHFR, (-), Preterm delivery (-), Inflammation (+), Hormones (+) Others- Insufficient data
A, D, E, K	**No**—K **Yes**—A, E **Maybe**—D	**No**—E, K **Yes**—If reserves depleted –A **Maybe**—D	**No**—D, E, K **Maybe**—A	**Yes**—A, D, E, K	Preterm delivery (- for **A, E),** Adolescence **(- A**), Parity (- **A**), Sun exposure (+ **D)**, Obesity (- D)
Minerals					
Iron, Copper, Zinc	No	No	No	No	Infant depends on hepatic reserves for iron needs
Calcium, Phosphorous, Magnesium, Iodine, Selenium	Yes	**No**—Calcium, Magnesium **Maybe**—Phosphorous, Selenium	**No**—Magnesium, Phosphorous **Yes**—Iodine, Selenium **Maybe**—Calcium	**No**—Calcium, Magnesium **Yes**—Iodine, Selenium **No Data**—Phosphorous	

TABLE 4 **Food groups which should be included in a lactating mother's diet**

Fruits and vegetables 2 + 3 cups	Half her plate *Fruits*— Fresh, frozen, canned, dried, 100% juice *Vegetables*— Dark green, red, orange vegetables, beans, peas, and starchy vegetables	DAILY INTAKE 2 cups = Fruits or 100% juice 3 cups = Vegetables
Grains 8 0z/ 227 gm	At least half of all grains eaten should be **Whole grains.** Whole grain bread, chapatis, brown rice, oatmeal, popcorn (**Not** microwave popcorn) **Oatmeal** (contain proteins, vitamins and minerals; Saponins, may increase breast milk production; contain β-glucans)	1 slice brown bread/ Whole wheat roti 1 cup ready to eat cereal ½ cup cooked pasta, rice, or cereal
Proteins 6.5 oz/184 gm	**Vegetarians**- Beans, peas, soy products, unsalted nuts, and seeds **Non-Vegetarian** – Seafood, lean meats, poultry & eggs **Seafood** provides excellent source of Omega-3 fats in the diet. Can have important health benefits for the baby and mother. Choose seafood with lower amounts of contaminants (methylmercury)	¼ cup cooked beans, ½ cup nuts or 1 tbsp peanut butter 1 ounce of lean meat, poultry or seafood 1 egg (piece of meat = palm of hand = 4 ounces)
Fats According to Dietary guidelines, fats should constitute 20–35% calories consumed	**Foods rich in PUFA** Walnuts, Sunflower seeds, Flax seeds or oil, Fish like salmon, mackerel, herring, albacore tuna, trout, Corn oil, Soybean, Safflower oil **Foods rich in MUFA** – Olives, Nuts (almonds, cashews, pecans, macadamia-a type of walnut), Canola oil, Avocado, Nut butter, Groundnut oil	1 tablespoon/day
Dairy 3 cups	Low fat milk, yoghurt, curds, cheese	1 cup milk ¾ cup curd/ yoghurt 2 small cubes natural cheese/ paneer Processed cheese (2 ounces) can be taken

TABLE 5 **Foods to avoid**

Trans fats	Baked foods, Microwave popcorns, Frozen pizza, Fried foods, Doughnuts, Fried chicken, French fries
Saturated fats Keep them to < 10% of calories/day	Fatty meat, processed meats like sausages, burgers, kebabs; coconut and palm oils, whole milk, white chocolate, toffees, cakes, pastries, biscuits, puddings, and pies
Excessive sea food Contains some amount of Mercury. Mercury damages the development, especially the brain, of the baby	Because of contamination with methylmercury. Mercury is a toxic metal that enters the water, and hence the seafood, soil, and the environment. The sources of mercury are Coal burning, cement production, small scale gold mining, dental amalgam, mining of coal and other metals. Forest fires (mercury incorporated in the plants is released in the atmosphere) Soil (through flooding) Volcano eruptions
Caffeine Limit to 2–3 cups/day	Passes from mother to the baby through breast milk Excessive intake causes irritability, poor sleeping patterns, fussiness, and jitteriness in the baby.
Sodas, Energy drinks, Tea, Chocolate	Contain caffeine

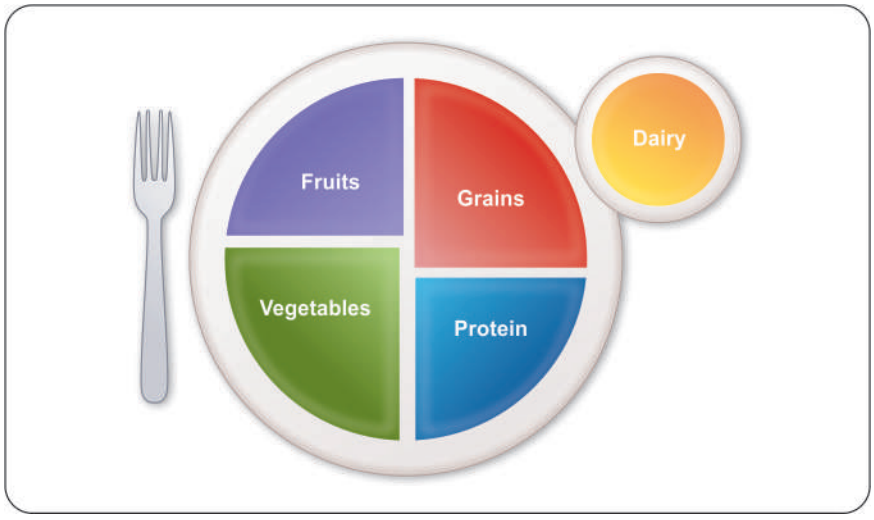

Fig. 1: Variety of foods adds to nutrition
Adapted from myPlate, USDA (US Department of Agriculture)

Frequently Asked Questions

1. *Do breastfeeding mothers need more calories?*[9]

Yes.

Approximately 450–500 kcal/day extra calories above the non-pregnant requirements are needed to fulfill the nutritional needs of the baby and to maintain their own health.

2. *Should multivitamins be taken during breastfeeding?*[9]

Yes.

Some people follow restricted diets (vegetarians, vegans, less number of calories—deliberate, or undernourished mothers in resource limited settings with <1500 kcal/day consumption). They are at risk of nutritional deficiencies themselves. Also, the Recommended Daily Allowances (RDAs) for some nutrients (like iodine) are INCREASED during breastfeeding and may not be fulfilled by diet alone. These mothers will benefit from taking multivitamins.

3. *Can I take GHEE during breastfeeding?*[8]

Yes.

Pure ghee, especially homemade from cow's milk is a staple in Indian diets. Literature review shows it contains antioxidants.

A 100 g of ghee contains 99.8 g of fats; Saturated fats—61.6 g, Trans fat—4 g, MUFA—28.7 g, Protein—0.2 g and Potassium—6.5 mg. It is a good source of energy, increases HDL and LDL (but no increase in Triglycerides or VLDL Cholesterol—the most harmful of the cholesterols. It can be taken in small amounts to take advantage of the antioxidants contained in it.

A maximum of 15 g/d = 1 tablespoon may be beneficial to the mother and the baby.

4. *Can I eat typical Indian foods like Date ladoos during breastfeeding?*[10]

Yes.

Typical Indian foods made for the lactating mothers in countries like India have multiple benefits for the mother, and hence for the baby. For example—

Date ladoo: Rich in Iron[10]

Methi ladoo: Proteins, iron, increases lactation (maybe because of the phytoestrogens present in the fenugreek leaves and seeds).[11]

Dink or Gondh ladoo: Acacia gum has a variety of health benefits. This is used in Ayurveda as an immunity booster, helps relieve constipation and is a natural antidepressant.

Ajwain Parantha (Carom seed parantha): Ajwain aids digestion and has antioxidants and biocidal value.[12]

Cumin Seeds (Jeera): Jeera is a rich source of antioxidants, scavenging activities, amino acids, alkaloids, flavonoids, essential FAs, PUFAs. It is considered beneficial to the mother and safe for the baby.[13]

Dalia Idli: Made of whole wheat. It contains fiber and vitamin E.

Hajira and Panjiri: Made from a mixture of highly nutritious Whole wheat atta, dry fruits, ghee, dink, etc. and can be consumed during lactation.

Aliv Kheer: Also called Haleem seeds or Garden cress seeds. These seeds have a balanced amount of PUFAs, MUFAs, vitamins A & E, eugenol, proteins, fat, dietary fiber, potassium, Oleic acid, Linolenic acid, Palmitic acid, Linoleic, erucic, stearic and Arachidonic acid. Hence, they are also immensely useful for the lactating mother.[14]

Ginger Candy: Ginger has potent medicinal compounds which have anticancer and antioxidant properties. It is also known as a galactagogue in Ayurveda. It can be taken safely during lactation.[15]

5. *What amount of alcohol is within safe limits for the baby during breastfeeding?*

None.

Even the smallest amount of alcohol should be avoided during breastfeeding.

Conclusion

Optimal somatic growth and metabolism in the baby is promoted by breast milk ingestion. Harmful microbes are destroyed, and their growth inhibited by known and unknown ingredients of human milk. Formula feeds have no such constituents.[16] The lactating mothers passes on all the ingredients benefiting the baby from her body—obtained either from her body stores which she has built up during her pregnancy, or from her diet. Hence, it is important to impress upon the mother and her care givers the importance of a healthy and nutritious diet for the mother for the benefit of both—the mother and the baby. The mother benefits by maintaining her health status. The baby benefits in multiple ways—a faster linear and head growth, better cognitive development, higher intelligence scores, enhanced responses to infection, lesser allergies, and better social adaptation. None of these advantages are provided by formula feed. Hence, in conclusion—

Yes! Eat Right, Baby Bright!!!

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Chapter 13

Fasting and Feasting

Nalini Anand

Introduction

- Can you fast? YES
- Is it unhealthy? No, it has enormous health benefits.
- Will you lose weight? Of course
- Is it difficult? Not really. But it's not exactly fun, either.

Let me explain some good facts about our cultural etiquettes, which need to be preserved and passed on to our next generation which are day by day losing its importance and values.

Fasting is not an obligation but it holds moral and spiritual value and aims to purify our body and mind and acquire divine grace…

Feasting means to have an elaborate and usually abundant meal often accompanied by a ceremony or entertainment…

Hippocrates wrote "To eat when you are sick, is to feed your illness"
Historian Plutarch wrote "Instead of using medicine, better fast today".
Ancient Greeks believed fasting improves cognitive abilities

Types of Fasts and Feasts since Ancient Times

- *Hindu fasts & feasts:* Day long fast (Karva chauth, Guru purnima), monthly (Ekadashi, purnima), longer fasts during Navaratri. Feasting during Diwali, Pongal, Dusshera, etc.
- *Islamic fasts & feasts:* Fast known as **Sawn** (Ramdan) and feast during **Iftar** (evening meal after breaking fasting).
- *Jain fasts & feasts:* Paryushan lasting 8 to 10 days. "Ratri bhojan tyag" (they abstain from food and water after sunset). They mark their feasting with ghee, sugar, jaggery made prasad during Diwali, New Year day, Mahavir Jayanti, etc.
- *Buddhist fasts & feasts:* Vassa or Buddhist lent is fast & feast observed for 3 lunar months every year (12 hr fast followed by 12 hr feast).

Here I would like to quote that "WEIGHT GAIN IS NOT ALWAYS STEADY, LARGELY HORMONAL AND NOT JUST A CALORIC IMBALANCE".

Certain periods of life are associated with increased weight gain:

- *Pregnancy:* Most dreadful condition in women's life which takes her metabolism up and down (it also increases the risk of obesity later in life as well).
- A 10-yearr follow-up data from *the first National Health & Nutrition Examination survey*—women's weight gain in those with children compared to nulliparous was 1.6 kg after adjustment.
- Similarly the *CARDIA STUDY* by the Journal of American Medical Association published that weight gain of 2–3 kg over 5 years associated with pregnancy.
- Menopause was associated with an average weight gain of 22.5 kg.

I'ts Natural Cycle of Life – Feast and Fast!!

A constant diet does not match the cycle of life. If you feast, you must fast. If you keep all the feasting and lose all the fasting, you get FAT. That's really not so hard to understand, is it?

Let me explain some physiology behind fasting as well as feasting…

Our body obtains energy from two different places, i.e., from:

- The food we eat
- Stored food energy

In fed state—insulin levels increase, no usage of stored food energy and insulin inhibits lipolysis and gluconeogenesis (normal physiology). In fasting state—insulin level falls, stored energy of liver (glycogen) is used and if that's not enough then from the body fat.

Some types[1] of fasting being studied these days are:

- *Calorie restriction:* If we talk in simple words, it means using of simple rule of reducing intake. As carbohydrates are major source of calories, we have to restrict them.
- *Intermittent fasting:* Many types in this particular section also. Either fasting on alternate days basis or fasting for some particular hours of the day where normal routine food intake can be taken and restricting intake in particular period of time.
- Time restricted eating/feeding is intake of food within a time window of 8–12 hours per day and fasting rest of the time.
- Periodic fasting is nothing but cycle of fasting or calorie restricted diets, for example—fasting 2 days per week, in which food intake is reduced to approximately 600 kcal and normal calorie intake on rest of the day.
- Long-term fasting is fasting for 2–21 days during which calorie intake of less than 200–250 kcal per day is maintained with appropriate schedule. Obese subjects and during the 1960s in morbidly obese subjects this type of fasting was very well practised successfully.

- Other regimens are the very-low-calorie-diets, a hypocaloric formula diet providing 80–100 g of proteins and an average of 1,000 kcal per day, formulated for obese and to avoid a negative nitrogen balance by using protein diet.
- *The fasting-mimicking diet:* In this hypocaloric diet (800–1,100 kcal), low protein, ketogenic diet leads to weight loss and to some of the effects of fasting. Nutrient restricted normocaloric diets like the ketogenic diet (carbohydrate restriction) and the protein or amino acid (methionine) restricted diet are being also intensively studied.

But we should always keep in mind that these diets should never be taken without proper medical guidance and monitoring.

Fasting Myths

- Fasting will lead to "starvation" mode.
- Fasting will make you more hungry.
- Fasting causes overeating when you resume feeding.
- Fasting deprives the body of nutrients.
- Makes you lose muscle.
- Causes hypoglycemia.
- Its just crazy!!
- Fainting due to starvation mode because of brain deprived of glucose

A big no… to this all.

It doesn't put you to starving mode... it helps you to use up your stored bad fat (that is LDL).

Doesn't overwhelm your hunger. Starvation mode is a bizarre ghost, always there to scare us away from missing even a single meal... just our own psychology of feel of more of hunger only during fasting... just an example that when you are busy in some work you neither feel thirsty nor hungry, why? Because you don't realize... but when you are fasting you always have an additional thought of that fact.

Again overeating is just your psychology to gain an additional energy which you haven't due to fasting...

Depriving our body of nutrients... again a BIG NO.

Muscles are built up by proteins and not fat... so again this is a MYTH.

Causes hypoglycemia? no... our body have a mechanism of gluconeogenesis which would never allow our body to have hypoglycemia during fasting if you have enough store of fat.

BRAIN FOOD – ONLY GLUCOSE?? Brain can use ketones in prolonged starvation as fuel source allowing storing protein in skeletal muscle. Fat is way of storing food energy for long term, glucose/glycogen is the short-term solution. Fat is not burnt when plenty of glucose is available as energy fuel in body.

Disadvantages of Fasting

- Patients especially diabetics go on fasting have to be monitored for blood sugar levels and adjust medications.
- Side effects of certain drugs on empty stomach, e.g., NSAIDs, Iron supplements, Metformin.
- Constipation.

Feasting

On a balanced diet containing good amount of carbohydrate, fat, and protein, our resting metabolic rate, body temperature, and respiratory quotient increase. Dietary components are utilized to replenish stores and augment glycogen and fat stores on body.

Excessive carbohydrates are converted into lipid in the liver and stored as triglycerides in adipose tissue (major fuel storage depot).

Amino acids in excess those needed for protein synthesis are preferably catabolized over glucose and fat for energy production.

If obesity & pregnancy are discussed then some complications that are commonly discussed would be as follows:

- General—fatigue, backache, depression.
- Surgical—hernia, gallstones, fat necrosis, difficulty in tracheal intubation, difficulty in spinal/epidural anesthesia.
- Obstetrical—miscarriage, stillbirths, PIH, type 2 DM, IUGR, preterm delivery, dystocia, prolonged labor, operative deliveries.
- New born—birth trauma, NTD, preterm birth, early neonatal deaths.

These all can be prevented just with practice of fasting in daily routine. Yes it is difficult to fast in today's world because we have forgotten our cultural values.

Not only obstetric but gynecological problems are also increasing due to obesity, some are mentioned below:

- Early onset of menarche.
- Adolescent menstrual problems—PCOD, oligo-hypomenorrhea
- Infertility
- Endometrial hyperplasia
- Hyperestrogenic state—fibroids
- Ovarian malignancy
- Vaginitis, vulvo vaginitis, UTI

What usually we advise our patients with above problem?

Let it be PCOS, infertility, vaginitis—we ask them to modify their lifestyle, we ask them to cut off their fatty food intake.

These all can be prevented just with simple practice of fasting.

Earlier Rishimunis use to fast just for sake of time saving so that they can utilize more of their time in worshipping and yagnas... but these modern era

needs fasting in order to save themselves from some dreadful diseases which are increasing these days just because of our bad food habits. Long-term fasting have been proven effective in order to reduce body weight along with abdominal circumference, which prevents us from going toward metabolic syndrome, cardiovascular diseases.

In today's era, more number of myocardial infarction, and venous sinus thrombosis are seen in younger patients, which were more common in people with age more than 60 years, just because of changing lifestyle and eating habits, which are altering our lipid profile. This can be prevented by just introducing one of the fasting types in our daily routine.

Yes, it is true we just cannot go on fasting haphazardly. So here again it comes how to manage?

Fasting and feasting both if done with a balance then it can really improve our lives.

Conclusion

Fasting in moderation is good but should be under medical supervision especially in cases of Diabetes, PCOS, and thyroid disorders etc., to acheive desired goals.

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Chapter 14

Probiotics in Obstetrics and Gynecology

JB Sharma, Parul Jaiswal

Introduction

Normal vagina comprise of secretions from various glands including sebaceous, sweat, Bartholin, and Skene; excretion from the vaginal wall, cervical mucosa, and endometrium; and micro-organisms along with metabolic products. Hormone levels determine the type and amount of vaginal secretions.[1] During menstrual cycle, there occurs an increase in the vaginal secretions due to concomitant increase in cervical mucosa.

The aerobic vaginal flora consists of different types of bacteria among which hydrogen peroxide-producing *lactobacilli* is the most common. The vaginal flora is determined by factors that assist in survival of the bacteria.[2] Vaginal pH and availability of glucose for metabolism of bacteria are the essential factors. Lactic acid helps in maintaining the pH of vagina less than 4.5. Vaginal epithelial cells which are responsive to estrogen are glycogen rich. There occurs breakdown of glycogen to monosaccharides in vaginal epithelial cells and *lactobacilli* to lactic acid.

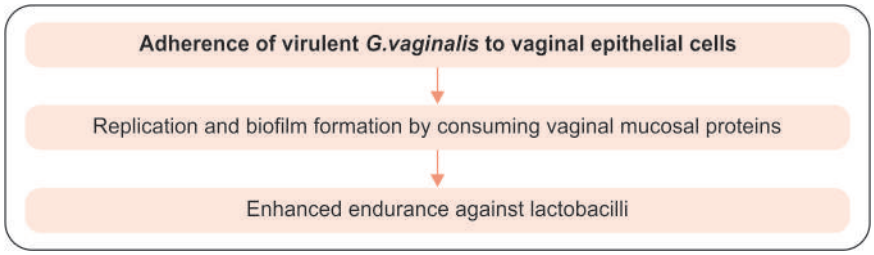
Normal vaginal secretions are flaky, white, and found in posterior fornix. Microscopy reveals presence of superficial epithelial cells, white cells, and clue cells. Bacteria like *Gardnerella vaginalis* attach to superficial vaginal epithelial cells and form Clue cells, seen under microscopy. Fungal elements in the secretions can be examined using potassium hydroxide 10%, which are negative in normal vaginal flora. Gram stain reveals normal superficial epithelial cells and a predominance of gram-positive rods (*lactobacilli*).

Normally commensal bacteria become pathogenic (e.g., *G. vaginalis, E. coli,* and *C. albicans*) when disequilibrium occurs. This occurs because of factors like hormones, repeated intercourse, douching, drugs, and vaginal hygiene. These aberrations can result in microbial disparity in the urogenital tract.

Urogenital Infections

Urogenital infections such as vulvovaginal candidiasis (VVC), bacterial vaginosis (BV), and urinary tract infections (UTI) affect billions of women each year, resulting in considerable morbidity and health-care costs.

Flowchart 1: Pathogenesis of bacterial vaginosis



- *Bacterial vaginosis* is a multimicrobial infection resulting in aberration of normal vaginal bacterial flora due to the loss of hydrogen peroxide as described in **Flowchart 1** producing *lactobacilli* and surplus growth of anaerobic bacteria.[3] Abnormal vaginal discharge is most commonly seen with BV. Less than 1% of normal women have flora comprising of anaerobic bacteria. In women with BV, anaerobic bacteria are substantially higher in amount in comparison to normal women and *lactobacilli* are usually absent. Symptoms include offensive smelling vagina, increased vaginal pH, and vaginal itching. These women are at increased risk for pelvic inflammatory disease, postoperative vault infections, and abnormal Pap results. BV complicates the pregnancy with premature rupture of membranes, preterm labor, chorioamnionitis, and post-cesarean endometritis.[4]
  Recurrence within 1 year of treatment are seen in around 50% of women. Some reasons for recurrence include the persistence of residual infection due to the formation of a biofilm that protects BV-causing bacteria from antimicrobial therapy, resistance due to poor adherence, and reinfection from either partners.
- *Trichomonas vaginitis* is caused by the sexually transmitted, flagellated parasite, *Trichomonas vaginalis*.[5] Around 60% of patients with trichomonas have accompanying BV. Patients with *T. vaginalis* infection are at an increased risk of HIV infection.
- *Vulvovaginal candidiasis:* It is the second most common infection after BV, caused by an over abundant growth of yeast cells, belonging to Candida species in vaginal mucosa. Seventy percent of women experience at least one episode of VVC once in their lifetime.[6] Few women experience chronic, recurrent infections, and is more common in pregnant women. *Candida albicans* is the most common organism associated with vaginal yeast infection. Other species of candida, such as *Candida glabrata* and *Candida tropicalis*, can cause resistant vulvovaginal symptoms. Pathogenesis have been explained in **Flowchart 2**. The extracellular toxin causes extensive itching and inflammation. Increased concentration of

Flowchart 2: Pathogenesis of vaginal candidiasis

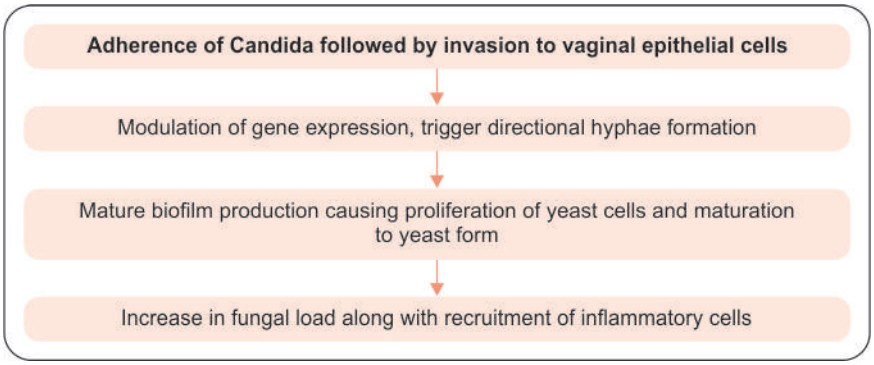


TABLE 1 **Risk factors for urogenital infections**

Bacterial vaginosis	Poor socioeconomic class, vaginal douching, smoking, multiple sex partners, unsafe intercourse
Vulvovaginal candidiasis	Multiple antibiotic use, pregnancy, uncontrolled diabetes, HIV, steroid use, immunosuppressive therapy

these micro-organisms (>10^4/mL) is found in symptomatic women as compared with asymptomatic patients (<10^3/mL). Risk factors have been summarized in **Table 1**.

Treatment

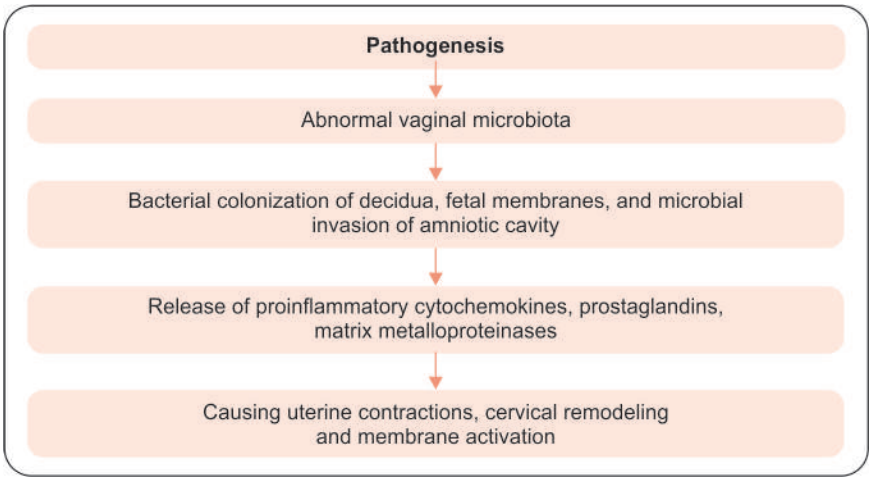
Bacterial vaginosis: Metronidazole is the drug of choice. Around 500 mg orally twice a day for 7 days or Metronidazole 0.75% gel, 5 gm intravaginally daily for 5 days or Clindamycin 2% cream, 5 gm intravaginally at bedtime for 7 days. Tablet tinidazole 2 gm orally once a day for 2 days is the alternative regimen. Metronidazole is safe for use in pregnancy.[7]

Vulvovaginal candidiasis: Fluconazole 150 mg single dose or topical azole therapy are used. Topical azole therapy for 7–14 days is given. Tablet fluconazole (100 mg, 150 mg, or 200 mg) on day 1, 4, and 7 followed by weekly for 6 months is given for recurrent VVC.

Urinary Tract Infection

It is estimated that millions of women suffer from UTI once in their lifetime. Multiple sexual intercourse and exposure to spermicidal agents predisposes to UTI.[8] Spermicides cause an increase in pH due to loss of *lactobacilli*. This causes the growth of gram-negative bacteria and subsequent UTI. *Escherichia*

Flowchart 3: Summary of causation of preterm labor by bacterial vaginosis



coli is the most common organism responsible for the symptomatic and asymptomatic UTIs. Vagina acts as a reservoir for bacteria responsible in the pathogenesis of UTI. There occurs proliferation of uropathogens in the vagina and peri-urethra, followed by ascending infection via the urethra to the bladder and seldom to the kidneys. An antibiotic course is treatment of choice for acute, symptomatic UTIs. However, rising rates of antibiotic resistance coupled with increasing UTI recurresnce call for the development of new and effective treatment strategies to combat their prevalence.

Dysbiosis in Pregnancy

During pregnancy, there occurs changes in vaginal flora causing predominant lactobacilli species and a decrease in overall diversity. Any pathologic changes make vagina susceptible to infections. Significant alterations in the vaginal flora, as explained in **Flowchart 3**, occur due to endocrine and metabolic changes of pregnancy, which increases the risks of preterm birth and other pregnancy adverse outcomes. One third of preterm birth cases occur due to ascending vaginal infections leading to intrauterine inflammation. Infection induced inflammatory pathways are thought to be the causal driver of around 40% of preterm births, and of as many as 80% of early preterm births before 28 weeks of gestation. BV is an important and independent risk factor for PTB.[9]

Dysbiosis and Reproductive Outcome

Infertility and microbiota have been found to be correlated in many studies. Many researchers have noticed that infertile women host a different microbiota. Poor implantation rates, poor pregnancy rates in

women undergoing in vitro fertilization (IVF) have been seen with vaginal dysbiosis especially in BV and incidence is as high as 19%.[10] BV may cause tubal infertility and abortion in women after IVF and may adversely affect the outcomes in IVF patients.

Probiotics Role in Urogenital Infections

Initial antimicrobial therapy may fail in up to 15% case and due to high recurrence rates, repeated usage of antibiotics may be needed.[11] This leads to production of resistant strains, alteration of vaginal flora, and proliferation of pathogens. Thus, it is important to maintain healthy vaginal microbiota. Probiotics are emerging as new treatment strategy for health maintenance. Repeated use of antimicrobials may result in elimination of commensal organisms, making vagina more susceptible to persistence of pathogens and leading to recurrent infections. Mechanism of action of probiotics have been summarized in **Table 2**. The main role of probiotics is to replenish the commensal organisms so as to decrease the risk of reinfections.

Lactobacillus lactis was first produced by Joseph Lister in 1878. *Bifidobacteria* was isolated in 1900 by a French pediatrician, Henry Tissier to treat infant diarrhea. Fermented milk products were found to increase survival by a Nobel Peace Prize winner, Elie Metchnikoff. Later, Alfred Nissle used *Escherichia coli* to treat and prevent shigellosis after being isolated from a non-infected soldier.[12] These 'live micro-organisms' were labeled as probiotics to provide health benefit to the host when administered.

TABLE 2 **Mechanism of action of probiotics**

Mechanism	*Action*
Direct bactericidal activity	Production of lactic acid, hydrogen peroxide
Reduction of energy substrate availability in the gut	Assist in fatty acid synthesis and glucose metabolism
Protection of epithelial cell (EC) barrier	• Inhibition of apoptosis and attenuated chemical damage • Intercellular tight junctions maintenance • Reduced production of toxins from pathogenic bacteria • Prevent attachment of Gram-negative bacilli to EC by producing oligosaccharides • Increased mucus production
Alteration of the host inflammatory response	• Reduces bacteria colonization • Increases secretion of IgA • Causes Down regulation of inflammatory process by changing expression of toll like receptors

TABLE 3 **Micro-organisms used in probiotics**

Micro-organism		*Species used*
Bacteria	Lactobacillus	*L. acidophilus, L. plantarum, L. casei, L. rhamnosus, L. cellobiosus, L. reuteri*
	Bifidobacterium	*B. bifidum, B. infantis, B. longum, B. thermophilus, B. animalis*
	Streptococcus	*S. lactis, S. cremoris, S. salivarius, S. intermedius*
	Leuconostoc	
	Pediococcus	
	Propionibacterium Bacillus	
	Enterococcus	*E. faecium*
Yeast and molds	Aspergillus	*A. saccharomyces, A. niger, A. oryzae*
	Candida	C. pintolepesii

Table 3 provides a list of micro-organsims used in probiotics. With increasing incidence of resistance to antibiotics, greater understanding of the mechanism and use of probiotics is prudent.

Probiotics in Vaginal Infections

Food supplements and yogurt have been found to have beneficial effects as probiotics.[13] Two criteria need to be met by the probiotic to be labeled as effective in treatment of urogenital infections:

- With minimum side effects, it should have ability to colonize in the host, and
- Urogenital pathogens must be inhibited by it.

BV can be prevented by the administration of probiotics. They have been found to cure BV, reduce its recurrence. They can be administered both orally and vaginally. Probiotics have the tendency to restore, analyze, and optimize the vaginal flora making it less susceptible to pathogenic organisms.

Probiotics in Preterm Birth

Probiotics prevents the ascending infection of BV and hence, provides protection against preterm birth. Pathogenic bacteria are inhibited from colonization by *lactobacilli. Lactobacilli* causes release of MMP-8 which inhibits the ascending infection to uterine cavity and invasion into amniotic fluid. Reduction in systemic inflammation due to inherent properties of probiotics leads to reduction in incidence of preterm.[14] Reduction in incidence of preterm delivery by 21% was found by Nordqvist on consumption of *lactobacilli* (milk product) in 37,050 women.

Probiotic in IVF

Probiotics represent an effective treatment for dysbiotic conditions affecting fertility. Restoration of the normal balance of the urogenital microbiota by oral supplementation of *lactobacilli* reduces the ascending infection by pathogenic bacteria. Live *lactobacilli* containing probiotics offer a safe choice of treatment.[15] *Lactobacillus* species, in particular, are helpful in the treatment of infertility, since they are the predominant micro-organisms of a healthy human vaginal microbiome and have been shown to prevent pathogenic infections associated with fertility and PTB.

Conclusion

Urogenital infections such as bacterial vaginosis (BV), vulvovaginal candidiasis (VVC), and urinary tract infections (UTI) hamper the quality of life of millions of women. BV makes the women susceptible to preterm labor and makes them more prone to sexually transmitted disease. Vaginal flora changes adversely affect fertility, reproductive outcomes, and poor implantation rates in women undergoing in vitro fertilization (IVF). Antimicrobial treatments are effective in the initial stages but are associated with antibiotic resistance due to over use and non-judicious exposure. Replenishing the normal microbes with use of probiotics help in combating the growth of pathogens and return to the lactobacilli dominated state. Due to their ability to produce antimicrobial compounds including bacteriocins, lactic and/or acetic acid, and hydrogen peroxide, they prevent adherence of pathogens to vaginal epithelium. Oral supplementations of probiotic capsules are particularly alluring because of their ease of use and high satisfaction versus the use of creams and gels.

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Chapter 15

Malnutrition and Immunity in Women

Jyoti Mary Jose, Prameela Menon

Introduction

Malnutrition refers to deficiencies, excesses, or imbalances in a person's intake of energy and/or nutrients. Though historically we have attributed the term malnourished to underweight or stunted individuals, the other end of the spectrum, obesity is becoming rampant all over the world including India. We as a population are becoming sick day by day and a large proportion of the adult population above 40 are on one or multiple drugs for chronic illnesses. The interesting fact is that this affects rich and poor alike. Nutrition science has been long neglected in even the medical curriculum. We have been taught to think about food as a kind of enriched fuel, a source of calories, and various nutrients which prevent disease and keep us healthy. In contrast, ancient people considered food as holy and eating was a sacrament to them as suggested by their prayers and songs. Focus on the individual nutrients has led us astray and popping a multivitamin or fortified highly processed "food like substances" on supermarket shelves have taken the place of whole fresh foods from nature.

Advances in the fields of microbiome research, epigenetics, nutrigenomics, proteomics, and metabolomics are changing the way we think of food. The ancient people were right, food is now emerging as a source of information for our body directing its myriad functions in ways unimaginable a decade or two back. It acts as information for your genes through modifying epigenetic pathways, it talks to your body through your microbiome and is capable of changing your mood, making you resistant or vulnerable to several chronic diseases, allergies, cancers, and infections by feeding the right or wrong microbes. Food also impacts your immunity through the microbiome-immune system crosstalk in the gut. In fact 70% of your immune system is found in the gut, which is the largest interface between the environment and your body. Food also acts as carriers of genetic information through micro-RNAs (mi-RNAs). It can stimulate or suppress stem cell activity and thus help in regeneration of damaged cells and organs. The wrong type of foods can stimulate unwanted growth of stem cells leading to tumors or cancers.

Defense Systems of the Body and the Influence of Diet

Microbiome

The gut microbiome has a huge role to play in the regulation of immune cell development and function. Mammals have co-evolved with these microorganisms across the span of millions of years. The gut microbiome which all of us are unwittingly hosts to, is a true example of a multicultural society based on mutualistic principles. The host provides the microorganisms with the ideal environment to thrive in. In return, these minuscule powerhouses take care of several physiological functions: digestion, homeostasis, improving immunity against pathogens, and even secreting essential neurotransmitters. No wonder the gut is often referred to as the second brain. Another function worth noting is the pro- or anti-inflammatory response signal derived from the gut microbiome that helps keep the immune cells on its toes, ultimately affecting the individual's susceptibility to diseases. The functions aforementioned only confirm how dependent we are on our invisible, omnipresent friends: the microbiome.

How many genes does the human genome contain? You would say, 23,000. What about an earthworm? 20,000. One would expect the human being, owing to its vast complexity, to possess many times more the number of genes that an earthworm possesses. But, apparently, the difference between the earthworm and the human genome is only about 3,000 genes, which is fascinating.

On the other hand, there are more than 100,000 proteins in our body, excluding those that are encoded by the microbial genome within us. The latest estimates say that there are about 38 trillion bacterial cells and only about 30 trillion human cells in the average human body.[1] That is a ratio of 1.3:1, bacterial cells to human cells.

The twist in the plot is that 84% of human cells are non-nucleated RBCs that cannot contribute genetically to the pool. Consequently, the genetic contribution of the microbiome is 10 times that of human cells. We are more microbial than human. Not surprisingly, we must draw the obvious conclusion that good microbiome is the key to good health.

We once considered the placenta to be a sterile area. Now, we know that even the placenta is home to unique microbiome. The fetus is colonized, even before its birth, by microorganisms transferred through the blood from the mother's mouth and gut. This throws light on the link between periodontitis and preterm labor.

The fetus on its way down the birth canal, through the mother's vagina and into the world, picks up microbiome from the mother's vaginal fluids and other secretions. The microbiome picked up by the baby on its way to the outside world, equips the little human to digest the mother's breastmilk.

The breastmilk goes onto provide the infant with other essential microbiome and human milk oligosaccharrides for these microorganisms to feed on.[2]

Early exposure to these commensal microbes is essential to the normal development of innate immunity, by training the baby's immune system to distinguish between the allies and the enemies.

Dysbiosis in early life has increasingly been associated with the disruption of the microbiome and its diplomatic defense strategy. This increases the individual's early predisposition to allergic disorders including asthma.[3] Maternal malnutrition and dysbiosis can result in long-term immunological malfunction in the offspring.[4]

High sugar, processed foods that are addictive at best, is consistently associated with dysbiosis. On the other hand, a diet rich in unprocessed whole foods, fiber, and microbiome is observed to be ideal. The fiber that is indigestible to the human gut alone is passed through the thriving civilization of microbiome that resides in our large intestine. Commensal microbiome feed on the fiber with relish, keeping our health intact in return. Microbial metabolites like SCFA (butyrate, propionate, and acetate) function as primary energy sources for luminal colon cells, especially distal segments **(Flowchart 1)**.

Angiogenesis

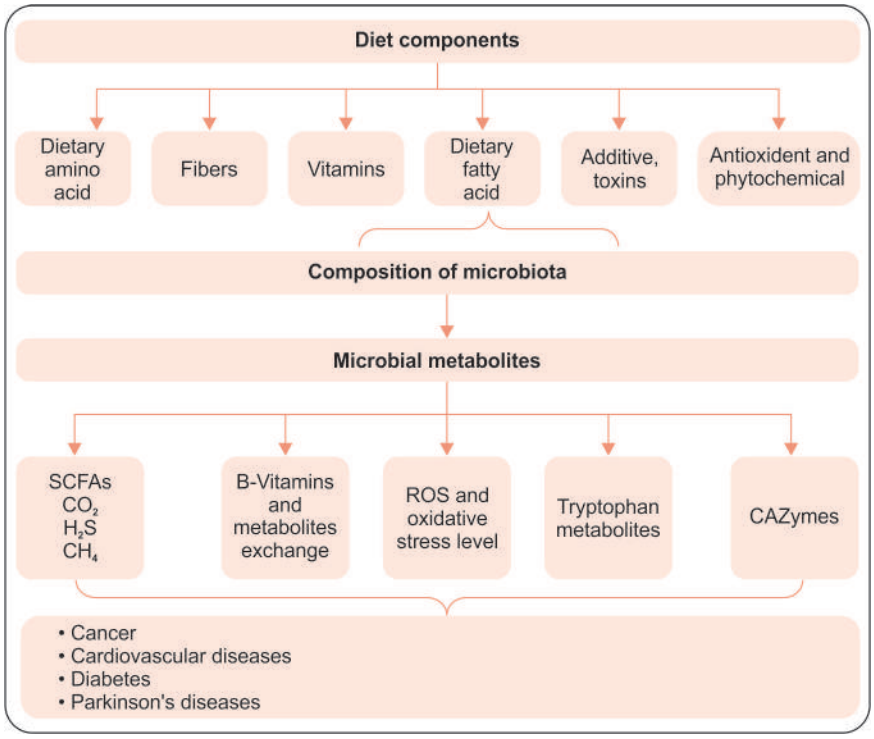
Autopsy studies show that 40% of women between the ages of 40–45 years had microscopic breast cancers and 50% of men between the years of 50–60 had microscopic prostate cancer and almost 100% above the age of 70 had microscopic thyroid cancer. These tumors are a result of mutations that occur within healthy cells due to environmental exposures. They may or may not develop into a malignancy. The line of balance is negotiated by several angiogenetic and anti-angiogenetic factors within the body. Unsurprisingly, diet has a huge role in the maintenance of this balance.

Plants contain bioactive compounds like *phytonutrients*[5] and several dietary proteins[6] that modulate angiogenesis. This fact can be used in diversifying therapeutic approaches to several problems, through nutrition. It is interesting to note that three proteins that are known modulators of angiogenesis are already present in breastmilk.

Insufficient and Excessive Angiogenesis

Excess and insufficiency of anything is harmful. Similarly, angiogenesis dependent disorders can be due to an excess or a lack of angiogenesis. Cardiac failure, ischemic tissue injury, slow healing gastric ulcers, organ dysfunction during pre-eclampsia, age-related diseases like nephropathy and bone loss, and other disorders like pulmonary fibrosis and emphysema

Flowchart 1: Interaction between diet composition and gut microbiota and its impact on gastrointestinal tract health



are related to insufficient angiogenetic signaling. Survival in stroke patients is also correlated with motor neuron degeneration associated with insufficient angiogenesis.

On the other hand, excessive angiogenesis results in disorders like cancers, arthritis, psoriasis, alzhiemers disease, age-related macular degeneration, endometriosis, scar keloids, asthma, and uterine bleeding. Recent studies have linked high-fat diets to increased angiogenetic signals which in turn stimulate adipogenesis.[7]

New research emphasises the relationship between diet and the modulating effects of bioactive compounds on angiogenesis. "This is the case of genistein, contained in soy; epigallocatechin 3-gallate, abundant in green tea; resveratrol, contained in wine; kahweol, present in unfiltered coffee; oleocanthal and hydroxytyrosol, two constituents of virgin extra olive oil; and carnosol and carnosic acid, two major components of rosemary extracts, among others."[8] Including the various herbs and spices which have been used for generations in traditional cuisines and following traditional cooking practices may thus help in strengthening this defense mechanism.

Stem Cells and Regeneration

Our bodies possess a wisdom that amazes us. Most cells and tissues in our body are capable of regeneration. We now understand that even the cardiac cells are reborn from endogenous progenitor cells in the heart, blood, and bone marrow cells.

The key to the much sought after fountain of youth is through the gut and the food we feed it. Research into the circadian rythms of our body is showing us that "when you eat is as important as what you eat".

Most religious or spiritual traditions of the world prescribe days of fasting to their followers, like the month of Ramadan or Easter. Modern science has now thrown light on how fasting can trigger stem cell regeneration.[9]

Tissue regeneration following damage as well as during homeostasis requires proper functioning of the immune system. Inflammation and immune cell recruitment are the first signs of early onset injury. Increased inflammation and excessive immune response has been shown to impede successful regeneration at the site of the injury. Balance is key.[10]

DNA Repair Mechanisms, Epigenetics, and the Role of mi-RNA

Our DNA is a library of genetic information and rather than an unchanging genetic code, it is always subjected to flux through environmental factors. The resulting damage if not healed, may further result in mutations and in disease.

The DNA is also subject to the action of metabolic byproducts and free radicals which may cause oxidative damage to the DNA. It is estimated that an individual cell can support around one million changes in its DNA in a single day.[11]

The relationship between the incidence of cancer and the consumption of fruit and vegetable (F&V) shows that these foods contain bioactive compounds with anticarcinogenic properties. Carotenoids, vitamins C & E, flavonoids, and polyphenols are antioxidants that neutralize the oxidative process. These fresh foods are also great sources of trace minerals that help in the synthesis of antioxidative enzymes like superoxide dismutase.

Phytochemicals like glucoraphanin, genistein, quercetin, and tangeretin found in *Brassica* vegetables, soy, and citrus fruits respectively, have been shown to modify carcinogen metabolism.[12]

Nutritional genomics is fast becoming an important field of study. It observes the interactions between the body and the components of a certain diet. An ideal example of a well-balanced diet is the Mediterranean diet which focuses on whole plant foods, seafood, monounsaturated lipids, low meat and dairy consumption, and a moderate intake of alcohol. This diet is hailed as a cultural heritage of humanity itself and has been known to prevent cancer.

"In a study published in the British Journal of Cancer (published by the research journal Nature) the researchers show that in laboratory tests, a compound called indole-3-carinol (I3C), found in broccoli, cauliflower, and cabbage, and a chemical called genistein, found in soy beans, can increase the levels of BRCA1 and BRCA2 proteins that repair damaged DNA."[13]

Mi-RNAs are a class of non-coding endogenous or exogenous (derived from the diet either of plant or animal origin) RNA molecules having ~22 nucleotides, which silences the mRNA and alters the gene expression.

Mi-RNAs are secreted by all plant, animal, bacterial, and fungal cells and are transported in virus sized membrane bound vesicles. Defying Mendels laws they can be transferred horizontally, across species, thus transferring genetic information. They escape digestion and act like software, altering the expression of the hardware, our protein encoding genes. A great example is the Chinese honeysuckle which has been used in Chinese medicine for treating viral influenza. A mRNA encoded by the honeysuckle actively inhibits influenza virus replication in host cells. Mi-RNA appeared to regulate responses related to both acquired and innate human immunity.

Nutrients like curcumin, reservatrol, quercetin, catechins, vitamin D, zinc, selenium etc. can modulate mi-RNA concentrations, acting as an important mechanism for the control of gene expression.

Considering the vertical transmission of mi-RNAs sourced through food, maternal nutrition has huge implications on fetal genetics. Parental malnutrition leads to epigenetic modifications of the infant's immune and metabolic genes.

Immune System: Innate and Adaptive

The immune system depends on the intake of both macronutrients, micronutrients, phytochemicals, and functional foods. Lipids like n-3 PUFA, zinc, vitamins D and E, probiotics etc. are some examples of dietary components that work together to improve immune function in the human body.

These nutritive and non-nutritive components of food have several essential functions such as the inhibition of proinflammatory mediators, promotion of anti-inflammatory functions and improved communication between the innate and adaptive immune systems. Vitamin D has been shown to highly influence the functioning of immune cells as well as the functioning of antigen-presenting cells (APC), which link the innate and adaptive immune systems.

Vitamin E deficiencies are also shown to result in impaired immune functions. Similarly, zinc, an essential micronutrient is required for normal growth, development, repair, metabolism, and maintenance of the cell health. Zinc deficiencies are estimated to affect 30% of the world population.

Selenium is also a trace element which has critical functional, structural, and enzymatic roles in a wide range of proteins as well as in the optimal functioning of the immune system. Deficiencies in selenium are often correlated with a high risk of several chronic diseases including cancer and cardiovascular disease.

Glutamine is a nonessential amino acid which is an important energy source for several cell types including immune cells. It also serves as a precursor to nucleotide synthesis, especially in the case of rapidly multiplying cells during an immune response. Immune cells consume glutamine at a rate higher than that of glucose, in the instance of an infection. Nutrients are capable of directly or indirectly modifying the immune behavior by initiating changes in the functions of the immune cells through the gutmicrobiome.[14]

The bioactive compound, n-3 PUFA, found in fish oil, is known for its anti-inflammatory properties as well as its role in the inhibition of inflammatory mediators. This compound is instrumental in the increased production of anti-inflammatory cytokines like IL-10.

Green tea is considered highly beneficial since it is rich in catechins like Epigallocatechin-3-Gallate (ECGC), which is the most abundant and the most biologically active. This compound serves in modulating multiple aspects of innate and adaptive immunity.[15]

The gut-associated lymphoid tissue (GALT) comprises of a majority of the immune cells within the human body. This reflects the importance of gut health in maintaining overall health. To protect the host against any threats that enter the body through food, the gut is armed with dendritic cells and M cells which sample the gut content. B cells, on the other hand, produce IgA, defending against pathogens. Specialized areas within the gut called Peyer's patches, rich in immune cells, facilitate communication between immune cells within the GALT and also between the gut and the wider, systemic immune system of the body.

The gut microbiome on the other hand provides antigens and signals which interact with the immune cells. As discussed earlier, the composition of the gut microbiome varies over time, according to dietary intake, environmental influences, and exposure to antibiotics.

Probiotics and prebiotics are dietary interventions that target the health of the gut microbiome. Probiotics are live microorganisms sourced through foods like yogurt and kimchi, which when consumed in adequate amounts, confer several health benefits. Prebiotics are those dietary components like non-digestible oligosaccharides and fructo-oligosaccharides which are selectively utilized by the gut microbes.

In certain circumstances, the immune cells of the GALT intercept nutrients or microbiome, in case of low gut epithelial integrity. This, consequently, results in what is known as the "leaky gut" syndrome **(Fig. 1)**.

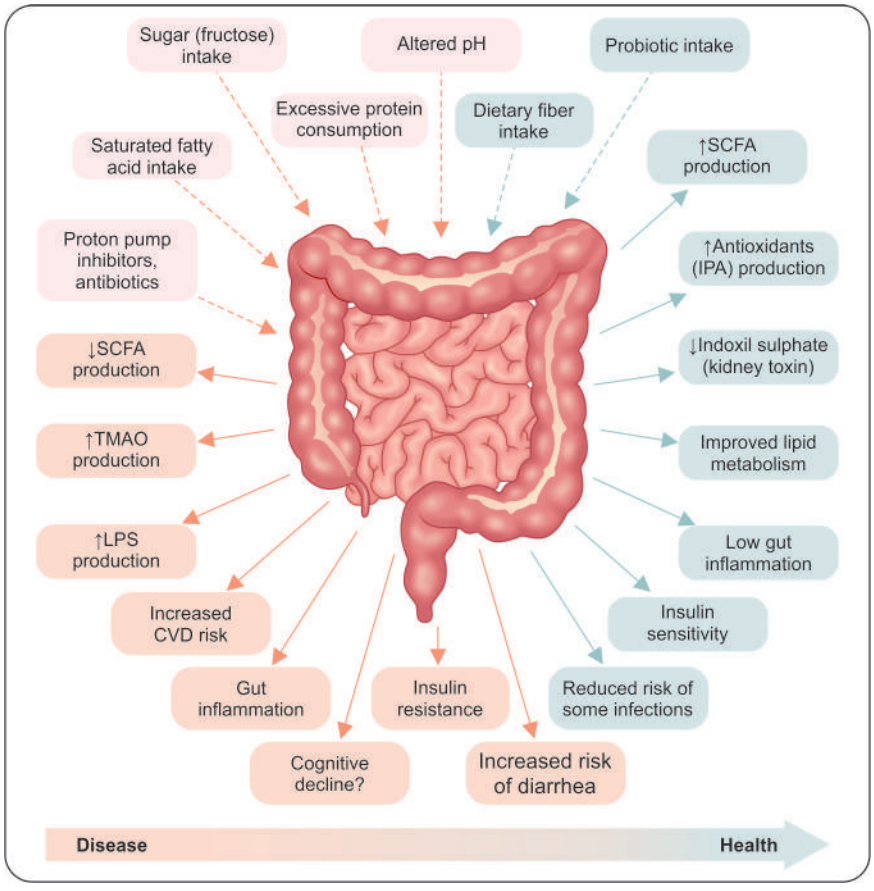


Fig. 1: Science and politics of nutrition
role of the gut microbiota in nutrition and health

Chronic inflammation caused by inappropriate immune responses and excessive growths of pathogenic gut bacteria is usually at the root of even seemingly unrelated disorders like cardiovascular disease, IBS, arthritis, psoriasis, arthritis, stroke, etc. Obesity and excessive nutrition is another factor which causes chronic metabolism-induced inflammation or meta-inflammation.

The regular American diet which is fast being imported to developing countries like India has a low content of complex carbohydrates, fiber, micronutrients, other bioactive molecules and genetic material.

Most processed and packaged foods contain added sugar which comes in various names like fructose, corn syrup, sucrose, etc. There are about 61 names which are used by the food industry to signify added sugar. Even seemingly healthy and clean products like baby formula and breakfast cereals contain these harmful sugary additions.

Fructose promotes insulin resistance, causing conditions like fatty liver. Processed foods containing these added sugars induce cravings and hunger pangs which eventually leads to obesity and/or diabetes. High blood sugar levels in diabetic patients are known to inhibit the angiogenetic process which leads to the diabetic neuropathy and chronic ulcers.

"The link between sugar and these diseases has been postulated to be at least partially through the gut microbiome. The implication is that increased consumption of existing sugars and novel sweeteners has altered the carbohydrate pools available to the microbiome, creating distinct environments in the gut that are filled by exogenous microbes or endogenous microbes that have undergone adaptation, some of which are pathogenic."[16]

Conclusion

The reductionist view of the human body as a complex machine, whose individual organs and components can be studied for its physiology and functions in isolation, has been replaced with the understanding that our health is an active state , with an array of defense mechanisms in place, to protect us from diseases. It is now well established that all organs of our body, including the brain has its own microbiome and is not sterile as we had been thinking. So also organs such as the heart and brain which had been considered as non-regenerating have been found to have stem cells within them which, given the proper environment (diet and lifestyle), are capable of regenerating.

The power of Food as medicine is now becoming more and more apparent. We doctors should take the responsibility of translating the vast amount of research in the field of nutrigenomics to common knowledge. There is no time to waste. It is time to take our healing into our own hands, through the choices we make as a consumer, each day.

This article is the fruit of information sourced from several sources including published research papers and the latest books on nutrition and immunity. The books that we have referred to, during the process of creating this article are listed below. We do hope that the reader finds it useful for further research. After all, this is not a question of curiosity but of survival.

- Obesity code Dr. Jason Fung
- Eat to Beat Disease Dr. William Li
- Regenerate SayerJi
- Deep Nutrition Catherin Shanahan MD

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Chapter 17

Vitamin D: The All Important Vitamin

Vijayalakshmi G Pillai

Introduction

Vitamin D is sometimes called the "Happy hormone". In fact, it can be considered a prohormone steroid which is converted to active "hormone". It is fat-soluble and is essential for maintaining our health. It is known to have endocrine, paracrine, and autocrine functions. Every cell in our body has a receptor for it. It is found in certain foods, e.g., fatty fish, fortified dairy products. It is unique in that; our body can synthesize it through the action of UVB light. This implies that, dietary reference intake value of vitamin D is not fixed. It is very difficult to get enough from diet alone. Body makes it from cholesterol when exposed to sunlight. Hence, the name "vitamin D", is a misnomer (Vitamin is conventionally defined as 'essential item getting through the diet').

Deficiency and insufficiency of vitamin D is the most common nutritional deficiency in man. It affects almost 50% of the population worldwide. Vitamin D deficiency in Indian subcontinent is considered to range 70–100%.[1]

Factors Influencing Vitamin D Deficiency

Dark skin, elderly (due to thinner skin), overweight or obese, insufficient dietary intake (vegetarian diet), living far from the equator where sun is less, using sunscreen, dressing methods, staying indoors, etc. influence vitamin D levels. Some factors alter absorption of vitamin D such as bariatric surgery, malabsorption syndromes, Celiac disease, chronic pancreatitis, cystic fibrosis, etc.

Black skin absorbs more UVB than white skin melanin. Pigmentation reduces vitamin D production in the skin. Hence, black skinned people require more sun exposure to produce the same amount of vitamin D. Ingested vitamin D is incorporated into chylomicrons, which go into the lymphatic system and enter the venous blood.

Vitamin D that comes from the skin or diet is biologically inert. Its first hydroxylation is in the liver by vit D-25-hydroxylase to 25(OH)D (Calcidiol).

This is further hydroxylated in kidneys by 25(OH)D-1 OHase (CYP27B1) to form the biologically active form of Calcitriol (1α,25(OH)2D3). Although 1α-hydroxylase is mainly seen in the kidneys, different extra-renal tissues also express this, like bones, colon, breasts, prostate, and placenta.

1,25(OH)2D3 (Calcitriol) accelerates intestinal calcium absorption. Without vitamin D, only 10–15% of dietary calcium and about 60% of phosphorus are absorbed. Thus, the endocrine effect of vitamin D is mainly maintenance of calcium homeostasis. The local production of 1,25(OH)2D may influence transcription of 200 to 2,000 genes (0.5–5% of human genome). This is the basis of the paracrine and autocrine effect of vitamin D. It is unique to different cell types depending on nuclear expression of vitamin D receptors.

Vitamin D deficiency (VDD) leads to increase risk of many diseases. It causes inhibition of cellular proliferation, promotes cell differentiation and apoptosis, inhibits angiogenesis, stimulates insulin production, inhibits renin production, and stimulates macrophage cathelicidin production. These may explain its roles in cancer, immunity, autoimmune diseases, cardiovascular and neurological disorders, and reproductive organ disorders and in pregnancy.

Why Vitamin D Is Important in Pregnancy?

Preeclamptic patients, patients with insulin resistance, and GDM all show increased vitamin D deficiency during pregnancy. VDD in mother is also seen to modulate immunity, and hence higher risk of preterm delivery, LBW, increased risk for cesarean section and impaired neonatal immunity.

Pregnancy and Global Magnitude of Vitamin D Deficiency

Vitamin D deficiency in pregnancy prevalence[2] of 33% in the US, 24% in Canada, 60% in India, 35% in the UK, 45% in Pakistan is seen in demographic studies of respective countries.

Vitamin D Metabolism in Pregnancy

Physiology

By 12 weeks of gestation, 1,25(OH)2D levels increase more than twice that of a nonpregnant adult. It reaches 2-3-fold from the nonpregnant baseline, rising to over 700 pmol/L. Vitamin D binding protein (VDBP) is increased and free 1,25(OH)2D levels also rise. Calcitonin rise during pregnancy stimulates renal 1-α-hydroxylase gene expression independent of calcium levels, but dependent on available 25-dihydroxyvitamin D levels. This is a unique feature of pregnancy that allows such high levels of 1,25-dihydroxy vitamin D. This implies an increased dietary intake to maintain the

increase serum levels. The human decidua can make 1,25(OH)2D and 24,25(OH)2D, while the placenta synthesizes only 24,25(OH)2D. Calcitriol aids implantation, maintains normal pregnancy, supports fetal growth, and limits production of proinflammatory cytokines. 24,25(OH)2D which accumulates in bone may be involved in fetal skeleton ossification.

Recommended Intake of Vitamin D during Pregnancy

According to 2012 NICE guidelines[3], all pregnant and breastfeeding women should have a daily supplement of 10 micrograms (400 IU) of vitamin D (1 micrograms is 40 IU). The three categories of women who require vitamin D supplementation are:

- general category,
- high risk category which has two subtypes, namely, high risk for pre-eclampsia & high risk for VDD, and
- vitamin D deficient women.

The recommended daily allowance of vitamin D in all categories are different as per NICE guideline. For general category 400 IU daily is recommended. High risk for VDD is recommended to take 1,000 IU daily; high risk for pre-eclampsia is recommended 800 IU daily. Treatment for already deficient women is either with cholecalciferol 20,000 IU a week or ergocalciferol 10,000 IU twice a week, for 4–6 weeks, followed by standard supplementation. According to Cochrane data review, which included several studies there is an evidence gap for the exact daily requirement of vitamin D in pregnancy and its potential advantages.

Vitamin D and Pre-Eclampsia

Maternal vitamin D deficiency in pregnancy and association with increased risk of pre-eclampsia[4] is known. It is also associated with new onset hypertension and proteinuria in pregnancy.[5]

Pathophysiology

An abnormal expression of 1α-hydroxylase is seen in pre-eclamptic pregnancies. This probably means a possible role for 1,25(OH) 2D3 as a regulator of placentation. IGF-1 (which is decreased in pre-eclamptic pregnancy) increases 1,25(OH) 2D production by syncytiotrophoblasts from placentae of normal pregnancies but not from pre-eclamptic pregnancies. Vitamin D's role as an endocrine suppressor in renin biosynthesis for the regulation of the renin-angiotensin system (RAS) is altered in pre-eclampsia. Vitamin D deficiency causes excess activity in Th-1 type cytokines. This decreases immunological tolerance to implantation and trigger pre-eclampsia. Further, vitamin D has angiogenic properties and VDD is associated with narrowing of spiral arteries leading to pre-eclampsia.[6]

Recommended intake for women at high risk of pre-eclampsia is 800 units a day in combination with calcium.[7]

Vitamin D and GDM

Maternal serum 1,25-hydroxy vitamin D3 concentration in GDM mothers at 24-28 weeks of gestation were significantly lower than non-GDM controls.[8] Significance of this is not sure. Association between development of GDM and hypovitaminosis D is not established in all studies. The data are all race-specific. Indian mothers do not seem to have an association between low vitamin D and GDM. The data so far do not support routine high-dose vitamin D supplementation for either the prevention or the treatment of GDM.

Pathophysiology

Vitamin D can influence glucose homeostasis in multiple ways. Pancreatic functions may be altered when immune cell infiltrate among glandular cells with a consequence of "inflammation". Vitamin D's anti-inflammatory properties helps to restore physiological insulin secretion. Vitamin D improves duodenal absorption and renal resorption of calcium which is available to the peripheral tissue intracellular signaling activated by insulin. Vitamin D has a direct effect on pancreatic beta cells. It increases transcription of insulin.[9] Calcitriol also stimulates the expression of insulin receptors. It helps to enhance insulin sensitivity by activating PPAR-δ (peroxisome proliferator-activated receptor delta). Many GDM patients are obese and obese patients have higher levels of vitamin D binding protein that can reduce bioactive form of vitamin D.

Vitamin D deficiency also leads to an increase in the levels of parathyroid hormone (PTH), which has been associated with insulin resistance.

Vitamin D and Low Birth Weight Babies

Cross sectional, descriptive analytical studies to assess neonatal anthropometric measurements in vitamin D deficient women[10] showed, at least in women who were overweight or obese before pregnancy, low 25(OH)D (<50 nmol/L) in both early and late pregnancy had impact on fetal development.

Although, pathophysiology of LBW babies is multifactorial and inadequate nutritional status is linked to the etiology of LBW, adequate vitamin D status during pregnancy is important for its prevention. Vitamin D is needed for fetal skeletal development, tooth enamel formation and general fetal growth and development through its interaction in Calcium homeostasis. Around 25–30 g of calcium is transferred to the fetal skeleton

in pregnancy. [11] Mannion et al. study showed that, for every additional 40 IU of maternal vitamin D intake, there was an associated 11-g increase in birth weight.[11]

Vitamin D and Preterm Births

Intrauterine inflammation and infection are the main causes of spontaneous preterm births. Studies have shown inverse association with Bacterial vaginosis and vitamin D deficiency. Maternal circulating 25-OHD levels of <50 nmol/L is shown to be associated with preterm deliveries. Vitamin D supplementation with 25-OHD to reach a serum concentration of 100 nmol/L could reduce the risk of PTB.[12]

Pathophysiology

Immunomodulation effect of 25-OHD protects against PTB. This is achieved by reducing intrauterine infection and inflammation by increasing the innate immune system. Cell-mediated immunity is altered by decreasing the secretion of inflammatory cytokines like IL-1, 6 and TNF-α that are known to be involved in spontaneous PTB. Vitamin D also helps to maintain myometrial quiescence. It reduces oxidative stress.

Vitamin D and Fetal Immunity

Low cord blood vitamin D concentrations are seen to be associated with respiratory and general infections in new born period. Neonatal vitamin D deficiency is linked to childhood asthma and other atopic diseases. The mechanism of action is not very clear.

Pathophysiology

Higher maternal vitamin D supplementation correlated well with gene expression of tolerogenic immunoglobulin-like transcripts 3 and 4 (ILT3 and ILT4). Vitamin D in cord blood quantity correlated positively with mononuclear cell release of IFN-γ and thereby Th1 cell development. This is proof for prenatal immune development and vitamin D adequacy status.

Vitamin D can up-regulate antimicrobial peptide production by macrophages and endothelial cells.

Mode of Delivery and Vitamin D

Very low maternal vitamin D levels, as low as <37.5 nmol/L, was associated with a significant rise in primary Cesarean deliveries. This could be due to the mother's poor pelvic muscle strength as well as uterine smooth muscle strength. This could lead to labor dystocia.

Vitamin D Screening and Supplementation in Pregnancy

There is no data supporting universal screening of vitamin D in pregnancy. For women at higher risk for vitamin D deficiency, maternal serum 25-hydroxyvitamin D levels can be checked. Vitamin D deficiency is currently considered as circulating 25-OH-D levels less than 32 ng/mL (80 nmol/L). An optimal serum level during pregnancy has not yet been determined. Vitamin D deficiency has to be interpreted based on clinical scenario. Vitamin D 10 micrograms (400 units) a day is recommended for all pregnant women who are at low risk for being deficient (RCOG Guideline).[7]

Experts agree that 1,000–2,000 IU per day of vitamin D is safe when treating deficiency. Upper limit of safe daily dose for vitamin D is highly variable. Different unsupported studies consider 4,000 IU to 10,000 IU daily, to be safe in pregnancy. Another regimen is to treat either with cholecalciferol 20,000 IU a week or Ergocalciferol 10,000 IU twice a week for up to 4 – 6 weeks. This has to be maintained with daily dose throughout the pregnancy.[13]

Vitamin D and Reproduction

Vitamin D receptor (VDR) is localized in both central and peripheral reproductive organs of male and female. VDR expressions in the brain are in the hypothalamus, pituitary, and the substantia nigra. In the male gonads, VDR and its metabolizing enzymes are found in the ducts, Sertoli and Leydig cells, germ cells, developing spermatozoa, and mature sperm.

Likewise, in the female, it is found throughout the reproductive tract (uterus and the ovary) and in placenta during pregnancy. VDR expression is seen in the promoter region of the AMH gene. Vitamin D deficiency is known to modulate of AMH levels.

Vitamin D and Endometriosis

Several studies have shown vitamin D to modulate the pathophysiology of endometriosis. Higher vitamin D receptor (VDR) and 1α-hydroxylase expression are seen in endometriosis.[14] There is an association between the level of vitamin D and severity of clinical endometriosis[15]—(25(OH)D3 serum levels are lower in women with severe endometriosis).[16,17] Studies have shown that vitamin D-binding protein (VDBP) polymorphisms and endometriosis[18] are also associated.

Vitamin D and Polycystic Ovary Syndrome

PCOS being the most common endocrinopathy in reproductive age-group women, several studies can be seen about its etiology. Lower level of vitamin D and insulin resistance[19,20] are known to go hand in hand. Obesity is known to be associated with low Vitamin D levels.[21,22] Serum hormone binding

globulin, as well as free androgen index and vitamin D levels[19,21] also have correlation.[21] Vitamin D supplementation improves clinical symptoms of PCOS like menstrual frequency[19] and metabolic parameters.

Uterine Leiomyomas

The exact pathophysiology of how Vitamin D is causative for fibroid development is not known. But it is known to inhibit growth of leiomyoma. Appropriate vitamin D level is known to induce apoptosis of leiomyoma cells.[23,24]

Low serum levels of vitamin D and symptomatic uterine leiomyomas[25-27] are known to occur. Uterine fibroid volume is seen to inversely correlate with vitamin D levels.

In Vitro Fertilization and Vitamin D

Although global rates of infertility have increased, its true implication with hypovitaminosis D is not very clear. IVF outcome and vitamin D levels have been extensively studied. The results are highly confusing. Majority studies have not suggested any significant correlation[28] in clinical outcome. Yet a few show associations of high clinical pregnancy rate (CPR) with high 25(OH)D concentrations.[29] Strong association of high serum and follicular fluid vitamin D concentration is shown.[30]

Vitamin D and Cancer

Several epidemiological studies on the role of vitamin D and its relation on incidence, mortality and survival rates for many cancers have been studied. The data available are mostly for breast, colorectal, ovarian, and prostate cancers, and vitamin D levels. Emerging evidence show the anti-cancer role of vitamin D and at least 17 cancers are likely to be vitamin D sensitive. Preclinical studies in the US shows,[31] 400 to 1,000 IU/day could reduce cancers by 7% for men, 9% for women.

Conclusion

Vitamin D has a key role in regulating the functions of female reproductive system. Vitamin D levels and its association with PCOS, endometriosis, uterine leiomyomas, and IVF outcome are shown in several studies. VDR expression is present in both central and peripheral reproductive organs. It has a definite role in modulating gonadal functions. The effect of vitamin D on gonadal function may be via affecting patterns of gene expression or could be direct.

Further preclinical and postclinical studies are required to establish vitamin D's role in treatment of female infertility and its several causative factors.

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Chapter 18

Role of Calcium in Women's Health

Shyamala Guruvare, Sanghamitra Paladugu

Introduction

Calcium is one of the six essential elements constituting 1.5% of total human body mass. It plays a major role in muscle and nerve physiology and bone mineralization. Nearly 98–99% of the body's calcium is deposited in the skeleton.[1]

Along with circulatory calcium (ionized form) that functions at a cellular level, the stored calcium which is deposited in the bones also is regulated by the Calcitriol (Vitamin D), Calcitonin, and Parathyroid hormones. The stored calcium is in the form of calcium hydroxyapatite, which is either deposited in bone or released in circulation depending on the circulating levels of calcium.[2]

Recent metabolomics studies have shown that this element has a vital role not only in bone health, but also in maintaining blood cholesterol levels, reducing obesity, and controlling blood pressure among women in all age groups. Accordingly, the actions of calcium are being studied in both reproductive and non-reproductive age groups.

Calcium Across Various Stages of Women's Life

Pre-pubertal and early reproductive life: During this period, the major function of calcium is in bone development. There is a constantly increased demand for calcium starting from infancy to early adult life. Absorption of calcium from the diet increases steadily and is maximum during the growth spurt, as about 40% of the skeletal mass is obtained during this period.[3] Adequate early deposition of calcium in the bones maintains the structural integrity of bone and reflects the bone strength in adulthood. WHO recommends 300–400 mg in infant life to 600 mg in childhood and about 1300 mg in adolescence and early adult life.[4] Calcium deficiency in early life when seen associated with vitamin D deficiency results in Rickets and osteomalacia.

Reproductive life: Deficient levels of Vitamin D and impaired Calcium metabolism is associated with difficulty in conception in many women.

Calcium levels have been identified to be negatively related to blood testosterone levels in women. Calcium metabolism has also been implicated in fecundity. Recently, lower calcium levels and lower Vitamin D levels were more frequently reported in women with PCOS than in women with other causes of infertility.[5]

Pregnancy

During pregnancy, the fetus obtains the necessary nutrition from the mother. Skeletonization of the fetus depends completely upon maternal sources of Calcium. There is also a twofold increase in absorption of calcium from the maternal gut to meet the needs of both mother and the fetus.

Calcium has been proven to reduce the incidence of hypertensive disorders of pregnancy.[6] The exact mechanism behind this has not been understood. Its action against endothelial cell activation is the most discussed mechanism. Also, calcium is postulated to act against the maternal immunological intolerance. In a recent study done as an extension of the WHO CAP trial (Calcium in preeclampsia), it was observed that in non-pregnant women with previous history of pre-eclampsia/eclampsia, after a period of low dose calcium supplementation, there was a baseline decrease in blood pressure.[7] This observation reiterated the role of calcium deficiency in cases of pre-eclampsia/eclampsia.

While it has been identified that gestational diabetes and insulin resistance have an immunological mechanism in the pathophysiology, calcium supplementation in addition to other minor minerals and Vitamin D was studied and proven helpful in GDM with a demonstrable reduction in the inflammatory markers and free radicals of oxidative stress.[8]

Adequate calcium supplementation is needed for fetal skeletal mineralization and growth. Its association with preterm birth is still controversial.[6] It has been proposed to act against inflammatory mediators released in infections which ultimately lead to preterm birth.

Lactation: During lactation to maintain the level of calcium in the breast milk, there is a steep rise in the release of calcium from the maternal bones.[9] There is also an observed reduction in bone mineral density; however, this reduction returns to normal after the infant is weaned off.

Premenopausal and menopausal age groups: Reduced estrogen levels in perimenopausal and menopausal age groups causes a drastic fall in bone mineral density in women. There is an exponential increase in bone turnover resulting in an imbalance between osteoblast and osteoclast activity. In response to the internal hormonal milieu, the excretion of calcium exceeds the absorption leading to a state of calcium depletion. In addition to these factors, genetic, environmental, and immunological factors combined,

women at this age group experience a continuum of calcium deficiency which in turn results in thinning of the bones, in other words osteopenia and osteoporosis.[10] Along with bone strength, calcium in older women has been shown to reduce the relative risk of hypertension and cardiovascular disorders.[11] Calcium has also been proven to mediate obesity and reduce cholesterol levels (LDL is reduced, and HDL is increased), by reducing the absorption of fatty acids and by activating lipid synthesis and storage.[12,13] Calcium also reduces the incidence of colorectal malignancies by reducing the absorption of bile acids.[14]

Human beings derive their major source of calcium from the diet, both dairy and non-dairy products. Dairy products rich in calcium are milk, yogurt, and cheese and non-dairy products include—nuts, vegetables like broccoli, kale.[15] Like any other nutrient, since food is the major source of calcium, the deficiency states of calcium are largely dependent on the dietary habits and quality of food consumed.[16]

There is a significant difference in daily intake of calcium worldwide with 200 mg/day in low income population groups to three times this number among high income population.[9] This disparity continued throughout the life of women and persisted even during pregnancy (650 mg/day vs. 950 mg/day).[9] Considering the beneficial role of Calcium in pregnancy WHO recommended 1.5–2 g of routine calcium supplementation among women of low income countries or in countries with a low dietary source of calcium.[6] Calcium supplementation among low income population in pregnancy has shown 30–40% risk reduction in pre-eclampsia when given after 20 weeks, along with a reduction in the severity of pre-eclampsia and further more by 30% when started preconceptionally and in early pregnancy.[4] On further studies, overall when calcium was compared with placebo there was a significant reduction in the incidence of pre-eclampsia especially in those women at high risk for pre-eclampsia and on low dietary calcium intake. When the same was extended to neonatal outcome, there was no correlation with preterm birth, low birth weight, neonatal death, or stillbirth. Also during pregnancy, there can be interaction with Iron supplementation, and hence both the drugs should be administered with some duration apart.[6]

Other than during pregnancy, there are still many controversies on Calcium supplementation at various age groups even for menopausal osteoporosis.[17] Among PCOS women, when used in conjunction with Vitamin D in induction cycles helps follicular maturation and ovulation. By its beneficiary effects on weight loss also, there is contribution to improve fertility outcomes in PCOS.[5]

However, it has been reiterated in most of the studies that improving the dietary source of calcium among others is the best method to prevent deficiency and related problems.[18] Calcium supplementation had been

suspected to increase the risk of renal stones, increase the risk of calcifications of tissues which included calcification of coronary vessels and heart valves.[19] Most of the studies gave controversial results in these aspects. Again, dietary source of calcium supplementation, though no beneficial role beyond a certain limit is devoid of these concerns.[20]

The most efficient way to increase the dietary source of calcium to meet the recommended daily requirements is to fortify foods with calcium.[21] Some of the European countries have recognized this as the need of the hour. Foods such as milk, flour, yogurt, and cheese have been fortified with calcium. Incorporating, such approaches in national nutrition programs, may help meet the development goals and covers a larger population.[22]

Conclusion

- Calcium is an essential mineral which in coordination with various hormones maintains the integrity of human skeleton.
- Has a beneficial role in PCOS, helps in follicular maturation, ovulation, weight loss.
- In pregnancy, calcium helps fetal skeletal mineralization, reduces incidence of gestational hypertension, reduces severity of pre-eclampsia, regulates the inflammatory mediators of GDM.
- In older age group of women, beneficial among obese helps in bone strength and offers protection against cardiovascular disorders.
- Food fortification with calcium is better a way to maintain calcium levels than supplementation.

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Chapter 19

Nutrition in Midlife and Menopause

Gurpreet Kaur Sandhu, Rajendra Singh Pardeshi

Introduction

Nutrition and diet play a significant part in the treatment of menopausal symptoms. The menopause is an opportunity to take care of yourself by adopting a healthy lifestyle to ease the transition into middle age. Changes in your diet and lifestyle will help you treat menopausal symptoms. Take advantage of this opportunity to examine your diet and strive to achieve a healthy balance. Exercising regularly and eating a healthy balanced diet including plenty of fruit and vegetables, Oily fish, and low-saturated fat diets can protect the heart and bones, avoid weight gain, and help ease challenging menopausal symptoms.

Menopause is a wake-up call for women that their bodies are shifting. This is a time to take care of yourself by making healthy lifestyle choices. Eating well and staying physically healthy will ease the transition into middle age. Women need about 200 fewer calories per day in 50s than they needed in their 30s and 40s. So, if the requirement is 2,000 calories/day, then 1,800 calories will be sufficient. Menopause is a period of a woman's life where her body undergoes changes that can result in weight gain. Around the same time, these developments promote the emergence of diseases known as diseases of affluence. Therefore, adequate management seems to be essential, and it should involve dietary, pharmacological treatment, depending on the patient's needs.

Since the risk of cardiovascular diseases, diabetes, and weight gain increases after menopause, it is critical to assist women in selecting a diet high in nutrients but low in caloric density, as well as selecting healthful fats, lean sources of protein, low-fat dairy or dairy substitutes, and plenty of fruits and vegetables. Women in their forties face several obstacles, including hormonal fluctuations that cause weight gain, loss of bone and muscle mass, and digestive issues; however, there is more they can do with the assistance of dietitians to begin a healthy transition into the postmenopausal years.

Counseling women on the benefits of eating nutrient-dense diets, consuming less calories due to lower energy demands, having sufficient

doses of vitamin D and calcium, and participating in physical activity such as aerobic and weight training exercise can help burn excess fat, develop muscle and bone, and avoid metabolic disease. Health professionals can help women understand that bodily changes begin long before midlife, and that they can benefit from learning what to expect and how to better avoid the harmful consequences of ageing.

Which foods to avoid in Menopause?

Cut back on high-fat foods. Use sugar and salt in moderation.

Limit alcohol to one or fewer drinks a day.

If you have hot flashes during menopause, you can find that avoiding such "cause" foods helps. Caffeine, spicy foods, and avoiding refined carbohydrates, added sugars, alcohol, caffeine, spicy foods, and salty foods can help relieve menopausal symptoms. Many women are concerned with the physical and mental changes that arise through the menopause process, and they become depressed because "eat less and workout more" does not produce results, making them vulnerable to diet cycling and disordered eating.

Menopause is a dynamic occurrence in a woman's body, and when combined with the symptoms of ageing, people require accurate and trustworthy knowledge to make good health choices. There are several vitamins, nutritional therapies, and diets available that provide non-hormonal recovery alternatives for women in their forties and fifties. Women want precise, dependable, and impartial knowledge on which to make health-related decisions.

Bone health: postmenopausal osteoporosis silent disease.

Phytochemicals used in fruits and vegetables are a good source of micronutrients for bone protection. Lycopene, a lipid-soluble carotenoid, has been shown in studies to guard against bone damage. Tomatoes and tomato derivatives are high in lycopene. Oxidative stress is associated with loss of bone mass. Antioxidants can prevent this loss. Lycopene is a potent antioxidant, found in tomatoes. Tomato-based food products have health-promoting and disease-preventing effects. Watermelon, pink grapefruit, and carrot are good dietary sources.

Lycopene: Lycopene reduced intracellular and mitochondrial reactive oxygen species (ROS) levels as well as the rate of oxygen intake.

Reduces the generation of ROS by macrophages and osteoclasts.

Regulates cell proliferation during bone remodeling. Downregulates the activity of NFkB. Nuclear factor kappa light chain enhancer of activated B cells is a transcription factor family that regulates many essential cellular behaviors, including inflammatory responses, cellular development, and apoptosis.

Reduces the release of inflammatory cytokines.

Enhances intercellular gap junctional communication.

Increases osteoblast differentiation.

Reduces osteoclast differentiation.

Calcium-rich food—spinach, moringa, brinjal, milk and milk products, broccoli.

Vit D3—fish, milk.

-Being euthyroid.

-Being physically active—weight bearing exercises are as important as nutrition.

Menopause Brain Fog

Many women feel forgetful or having a general BRAIN FOG. That makes it hard to concentrate. Are memory issues part of menopause?

Yes, and this brain fog is more common than we might think.

Menopausal women often complain of "brain fog," or forgetfulness, as well as difficulties focusing and thinking clearly. Although these complaints are anecdotal, some tests have demonstrated that they can be statistically detected.

Eight top foods to beat menopause brain fog:

- Green leafy vegetables
- Fatty fish
- Berries
- Walnuts
- Flax seeds
- Avocados
- Broccoli
- Turmeric

Green leafy vegetables: Kale, spinach, collard greens, and mustard greens are high in lutein and zeaxanthin, which can help protect our eyesight and memory as we get older.

A 5-year survey of 950 older adults showed that those who consumed at least two portions of dark leafy greens per day had a slower loss in brain activity than those who did not consume any leafy greens.

Fatty fish, such as salmon, halibut, mackerel, sardines, and tuna, are high in the omega 3 fatty acids EPA and DHA. In cases of mild Alzheimer's disease and severe depression, it is beneficial in improving brain control. As an alternative to seafood, algae-derived EPA and DHA supplements are a better source of brain-boosting omega 3 fats.

Berries, such as strawberries, blackberries, and blueberries, contain antioxidants that may aid in weight loss, disease prevention, and inflammation

reduction. Berries are also abundant in anthocyanins, which are antioxidant-rich pigments that lend them their purple, red, and blue hues. Anthocyanins have been shown to successfully counteract age-related deficiencies in specific aspects of working memory. Neuroinflammation is inhibited, neuronal signaling is activated, and blood supply to the brain is improved.

Walnuts: A decent supply of alpha linolenic acid (ALA), an omega 3 fat, as well as other brain-healthy compounds. For 2 years, they consumed 15% of their calories from walnuts, which postponed the start of cognitive loss. Walnuts can actually enhance nerve connectivity in the brain, while also reducing inflammation and stimulating the formation of new neuron pathways.

Flaxseeds are the best plant-based source of antioxidants and are high in ALA, an omega 3 fat and precursor to EPA and DHA. Consume ground flaxseed rather than entire flaxseed because it is more easily ingested. Flaxseed oil has been found to increase the levels of neurotransmitters in the brain.

Avocados: Intake of avocados has been found to increase the density of lutein in the brain. Memory, concentration, and problem-solving abilities were also enhanced in the Avocado community.

Broccoli: High in ALA, vitamin K, and choline, broccoli will help keep your mind sharp.

Choline helps to improve adult brain function, prevent age-related memory loss, and have neuroprotective implications in degenerative brain disorders such as Alzheimer's.

Turmeric: An Indian spice distinguished by its bright yellow-orange color; turmeric has potent medicinal properties. Combining curcumin with black pepper, which includes the element Piperine, is associated with a 2,000% improvement in curcumin bioavailability.

Eat a well-balanced diet: Since it is high in omega 3 fatty acids and other unsaturated fats, the Mediterranean diet, for example, can benefit brain health.

Good food choices include:

- Fresh fruits and vegetables
- Whole grains
- Fish
- Beans and nuts
- Olive oil

How to Live a Colorful Life: Incorporating a diverse range of colorful plant foods on a regular basis can not only make you feel healthier and increase your overall health. It may also be beneficial to our brain.

How can insomnia be avoided?

Insomnia affects 61% of postmenopausal women.

Avoid eating large meals before bedtime.

Spicy or acidic foods may cause hot flashes. Avoid caffeine, alcohol, and nicotine before bed. Don't wear heavy clothing.

Work on relaxation/meditation.

Stress can make snoozing even more difficult.

Try deep breathing exercises, yoga, or massage.

Increased abdominal visceral fat is a part of menopause.

An energy deficit of 500 kcal/day should result in an approximate 500 g loss per week.

Low fat and carbohydrate diet.

Very low energy diet. One should avoid trans fatty acids as they are more dangerous than saturated fats. Avoid biscuits prepared with trans fatty acids.

A 2% rise in trans-fat energy consumption has been linked to a 23% increase in the incidence of heart disease.

Repeated heating/frying led to an increase in trans-fat content.

FSSAI clearly states that oil should not be reused more than 2–3 times.

Coconut oil is rich in medium chained triglycerides that are largely used by the body for production of energy. Hence, the chance for it to be stored in our body is less likely.

It is exceptional at helping people lose abdominal fat.

Oats

Oats contain beta glucan, which is a soluble fiber that helps bring down cholesterol level especially LDL (bad cholesterol) in the body.

Can sarcopenia be prevented/treated with diet modification?

Proteins play important role in sarcopenia. Ageing is associated with a reduced ability to stimulate skeletal muscle protein synthesis in response to feeding, insulin, and resistance exercise. To prevent or slow sarcopenic muscle loss, clinicians should stress the importance of ingesting a sufficient amount of protein with each meal. To maximize muscle protein synthesis whereas being cognizant of total energy intake, a dietary plan that includes 25–30 g of high-quality protein per meal.

Whey protein improves muscle mass and insulin sensitivity in older adults. Whey protein consumption leads to greater increase in MPS (mean protein synthesis) than other proteins due to its rich leucine content.

Whey protein has been shown to enhance lean mass in numerous populations including young, older adults, and PD/T2D [pre-diabetes (PD) and type II diabetes (T2D)] as well as preserve muscle anabolism and lean body mass during weight loss. Whey protein resulted in a greater loss of body weight and fat mass and a smaller loss of lean mass.

MPS (Muscle Protein Synthesis) and MPB (Muscle Protein Breakdown)

Phytoestrogens: are plant-based estrogens.

Phytoestrogens are hormone-like diphenolic compounds obtained from plants. These compounds are mildly estrogenic and can play a role in the prevention of other diseases.

Cardiovascular disorders, menopausal complications, postmenopausal osteoporosis, neuroprotective effects, and hormone-dependent cancers are all estrogen-related problems.

(Endometrium and breast cancer)

These are nonsteroidal, naturally occurring phenolic compounds classified into two groups: flavonoids, which are further subdivided into isoflavones, coumestans, and prenyl flavonoids; and secondly, the nonflavonoids, comprising the lignans. All are polyphenols that have a structural similarity to estradiol and possess estrogenic activity due to having a similar to estradiol's ring and containing two hydroxyl groups at positions that allow for the proper distance between them to enable binding to the ER.

Isoflavones are absorbed faster than lignans, while lignans are removed later.

Over a 24-hour cycle, the combination of both molecules will ensure a greater reduction of postmenopausal symptoms.

Calcium and vitamin D-fracture risk: Dairy products enriched with calcium and vitamin D improve bone mineral density.

Sufficient calcium intake (in the presence of adequate vitamin D status) has been shown to prevent bone deterioration and fractures in peri- and postmenopausal women.

Women above the age of 60 who are postmenopausal who have insufficient calcium intake. Calcium exerts a heavy influence.

Enhances the Bone-protective Effects of ET/EPT (ET-Estrogen Therapy, EPT-Combined Therapy)

Among postmenopausal women (estrogen-progestogen therapy). Calcium supplementation is regarded as a critical component of any clinical plan for patients with proven osteoporosis.

During menopause, a woman's calcium requirement rises (or whenever estrogen is lost). This is due to the fact that calcium absorption performance and renal conservation are both estrogen dependent and deteriorate in an estrogen-deficient state. Postmenopausal women should consume 1,200 mg of calcium a day.

To reap the nutritional benefits of calcium, you must have adequate vitamin D status, which is described as serum 25(OH)D of 30 ng/mL or

higher. This degree is usually attained by a normal oral intake of at least 400 to 600 IU.

Calcium can be obtained primarily by food. Dairy products are among the best calcium sources due to their calcium content, absorption, other essential nutrient content, and low cost compared to overall nutritional value. The 1,200-mg target is met by eating approximately 3 cups of dairy products a day.

Supplements and fortified diets provide an alternate source for women who are unable to eat adequate dietary calcium to meet the RDA. To improve absorption, calcium supplements should be taken with meals and in divided doses (typically 500 mg or less at one time). Since calcium bioavailability varies by product, name-brand supplements that have been checked for stable bioavailability are suggested.

In postmenopausal women, calcium and vitamin D supplementation can help avoid osteoporosis hip fracture.

In moderately stable postmenopausal women, higher calcium (800 mg a day) and vitamin D (600 IU) consumption avoided osteoporosis.

Indian diet is menopause friendly!

- Fennel seeds: to combat hot flashes (estrogenic effect)
- Cardamom: to mitigate menopausal symptoms (estrogenic effect)
- *Garlic:* Improves bone and joint health, muscle health (anti-inflammatory effect)
- Moringa leaves: to mitigate menopausal symptoms and improve overall health

Remedies for Hot Flashes

Evening primrose oil, vitamin E, sage, flaxseeds, soy, vinegar.

Evidences: Cochrane review (2012) evaluated 16 RCTs on the effectiveness of black cohosh in reducing menopausal symptoms. There is actually evidence to justify the use of black cohosh in the treatment of menopausal symptoms.

However, further studies in this area are needed. ACOG (2015) Clinical guidelines for managing menopausal symptoms concluded that herbal dietary supplements like black cohosh is efficacious for the treatment of vasomotor symptoms.

Black cohosh: Black cohosh is a flowering plant, a member of buttercup family that's native to North America. Its scientific names are Actaea racemosa and Cimicifuga racemosa, and it's Black bugbane is also known as black snakeroot, baneberry, and fairy candle. Some studies Black cohosh has been found to alleviate menopausal problems such as hot flashes.

Black cohosh is a herb that is often used to relieve menopausal and perimenopausal effects.

These signs include, in particular, hot sweats, moodiness, vaginal dryness, and heavy sweating. Roots and underground stem, rhizome have antioxidant, anti-inflammatory properties and have effect similar to SERMS. Available as powder, liquid extract, pills.

Seven ways to relieve menopausal symptoms: Ginseng, chasteberry, red clover, garlic, green tea, red clover, and black cohosh.

Nine easy measures to lower menopausal symptoms:

- A calcium and vitamin D-rich diet is important for preventing bone loss during menopause. Since calcium and vitamin D are related to bone health, it's important to have enough of these nutrients in your diet.
- Achieving and keeping a healthy body can assist with menopause symptoms and disease prevention.
- A diet high in fruits and vegetables can help keep bones healthy while also preventing weight gain and some diseases.
- Hot flashes, night sweats, and mood swings can be triggered by some foods and drinks. Caffeine, alcohol, and sugary or spicy dishes are examples of this.
- Proper exercise may help relieve menopausal symptoms such as insomnia, nausea, depression, and exhaustion. It may also help to prevent weight gain as well as a variety of illnesses and conditions.
- Foods that are high in phytoestrogens can have minor advantages for hot flashes and the major risk factor for heart failure. However, the proof is conflicting.
- Drinking plenty of water can help prevent weight gain, assist in weight loss, and alleviate dryness symptoms.
- Diets rich in packaged foods and refined carbohydrates have been linked to an increased risk of depression and poor bone health in postmenopausal women.
- Regular consumption of high-quality protein can help prevent lean muscle loss, assist in weight loss, and control mood and sleep.

Who Are the People Likely to Get?

Women with thyroid dysfunction. Common in black race least reported among Asian women. High BMI and smoking are risk factors.

How Do You Explain Hot Flashes?

A hot flash is a sudden sensation of temperature in the upper body, most notably over the face, throat, and chest. Your skin can flush, as though you're blushing. Sweating can also be caused by a hot flash. You can feel chilled if you lose so much body heat. Hot flashes are most often triggered by hormonal fluctuations before, and after menopause. It is unclear how

hormone variations trigger hot flashes. Hot flashes arise as the body's estrogen levels drop.

To make the thermostat (hypothalamus) more alert to small variations in body temperature. When the hypothalamus believes the body is warm, it sets in motion a series of events—a hot flash—to calm you off. Hot flashes sometimes occur unexpectedly, but the duration of each hot flash varies. Some hot flashes last just a few seconds, while others will last up to 10 minutes. Hot flashes last about 4 minutes on average.

Hormone Replacement Therapy (HRT)

HRT has risen and fallen in popularity over the years. Synthetic hormone therapy could be an alternative for certain women whose hot sweats are painful and have a negative impact on their quality of life.

Blow Hot-Blow Cold, during Menopause

A hot flash is a spontaneous sensation of temperature in the upper body, most notably over the face, throat, and chest. The skin can turn red, as though the individual is blushing. Palpitation and perspiration follow, each hot flash may last 5 long minutes, up to 20–30 times a day. Accompanying anxiety worsens the experience, can disrupt daily activity, and sleep may last for 7–10 years after menopause.

Menopause is thicker than water. We understand and enjoy as we talk about it and joke about it. It's a life transition not a disease.

Conclusion

Exercising regularly and eating a healthy balanced diet including plenty of fruits and vegetables, oily fish, and low-saturated fat diets can protect the heart and bones, avoid weight gain, and help ease challenging menopausal symptoms. Counseling women on the benefits of eating nutrient-dense diets, consuming less calories due to lower energy demands, having sufficient doses of vitamin D and calcium, and participating in physical activity such as aerobic and weight training exercise can help burn excess fat, develop muscle and bone, and avoid metabolic disease. Caffeine and avoiding refined carbohydrates, added sugars, alcohol, spicy foods, and salty foods can help relieve menopausal symptoms.

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Chapter 20

Micronutrients in Infertility

MG Hiremath, Rekha Rajendrakumar

Introduction

Food that we eat are not always packed with all the nutrients that are essential for the effective working of our systems. Thanks to the change in the methods of farming and the chemicals being added to the soil, the depletion of natural minerals due to over-farming and the various kinds of atmospheric pollution, etc., we do not get proper nutrition and that is the reason food supplements are the need of the hour.

Adequate levels of nutrients and micronutrient supplements are important to restore both male and female infertility like sperm morphology and motility, oocyte quality, maturation, fertilization, and implantation and thus to optimize the reproductive health, whereas antioxidants are vital to reduce oxidative stress.[1] Commonly studied supplemental and dietary antioxidants include vitamin D, vitamin E, vitamin C, β-carotene, and coenzyme Q10. Studies have shown that higher intake of iron, folic acid, and vitamins D and E may play a beneficial role in female infertility. Vitamins B_6, B_{12}, and iron all have roles in mechanisms that could affect fertility, including homocysteine metabolism, inflammation, oxidative stress, and embryogenesis. Regular use of multivitamin supplements may decrease risk of ovulatory infertility.[2]

Supplementation with micronutrients may be a good strategy to adopt in healthy women trying to conceive and in those with fertility problems. The importance of nutrition at a molecular level is well established as numerous processes in DNA synthesis are dependent on minerals such as zinc, copper, and selenium, as well as vitamin B, folate, and other antioxidants. Adequate intake of antioxidants supports female reproductive functions along with the intake of dietary supplements containing folic acid, β-carotene, vitamin C and E, which are definitely efficient in shortening the time to conception.

Female Infertility

Vitamin D

Vitamin D is an emerging factor influencing female fertility and IVF outcome and its supplementation yields higher success rate in IVF. High prevalence of vitamin D deficiency was noted in infertile women referred to ART centers. Vitamin D deficiency is contributory to ovulatory infertility. Vitamin D has direct effect on AMH production, and thus increases longer maintenance of ovarian reserve with its higher concentration. Vitamin D improves embryogenesis and pregnancy rates in infertile women undergoing IVF/ICSI.

It improves insulin sensitivity in PCOS patients.[3] Higher vitamin D levels are associated with an increased likelihood of successful pregnancy and may be of particular benefit to women with PCOS in lowering hyperandrogenism. Its supplementation helps in prevention of gestational diabetes and pre-eclampsia. Low levels of 25(OH) vitamin D were significantly associated with autoimmune thyroid disease in women with PCOS.

It acts as an immunomodulator in treatment of recurrent miscarriage.[4] **Figure 1**, explains the role of various micronutrients, and how the deficiency of certain micronutrients like vitamin D contributes to the pathogenesis of PCOS.

Hyperhomocysteinemia

Vitamin B6, B12, & folic acid reduce the concentration of homocysteine. Hyperhomocysteinemia causes decreased probability of conception, increased chances of placental abruption and increased risk of early recurrent pregnancy loss.[5] B-group vitamins and folic acid administration counteract the Hcy-increasing effect seen with metformin therapy. In PCOS patients who were given 2 g myoinositol with 200 µg folic acid daily for 12 weeks, a significant improvement in hormonal parameters and restoration of menstrual cycle in all patients with amenorrhea and oligomenorrhea was observed.[6]

Folic Acid

Promoting healthy dietary patterns and higher folate intake among individuals experiencing infertility may improve their chances of achieving a pregnancy. Folic acid is important for oocyte quality and maturation, implantation, placentation, fetal growth, and organ development. Sub-fertile women who took a multivitamin containing 400 µg of folic acid for 3 months, 26% had a pregnancy compared to 10% of women in the placebo group.[7] Evidence suggests that higher consumption of pre-pregnancy folate may lower the risk of some infertility outcomes.[8]

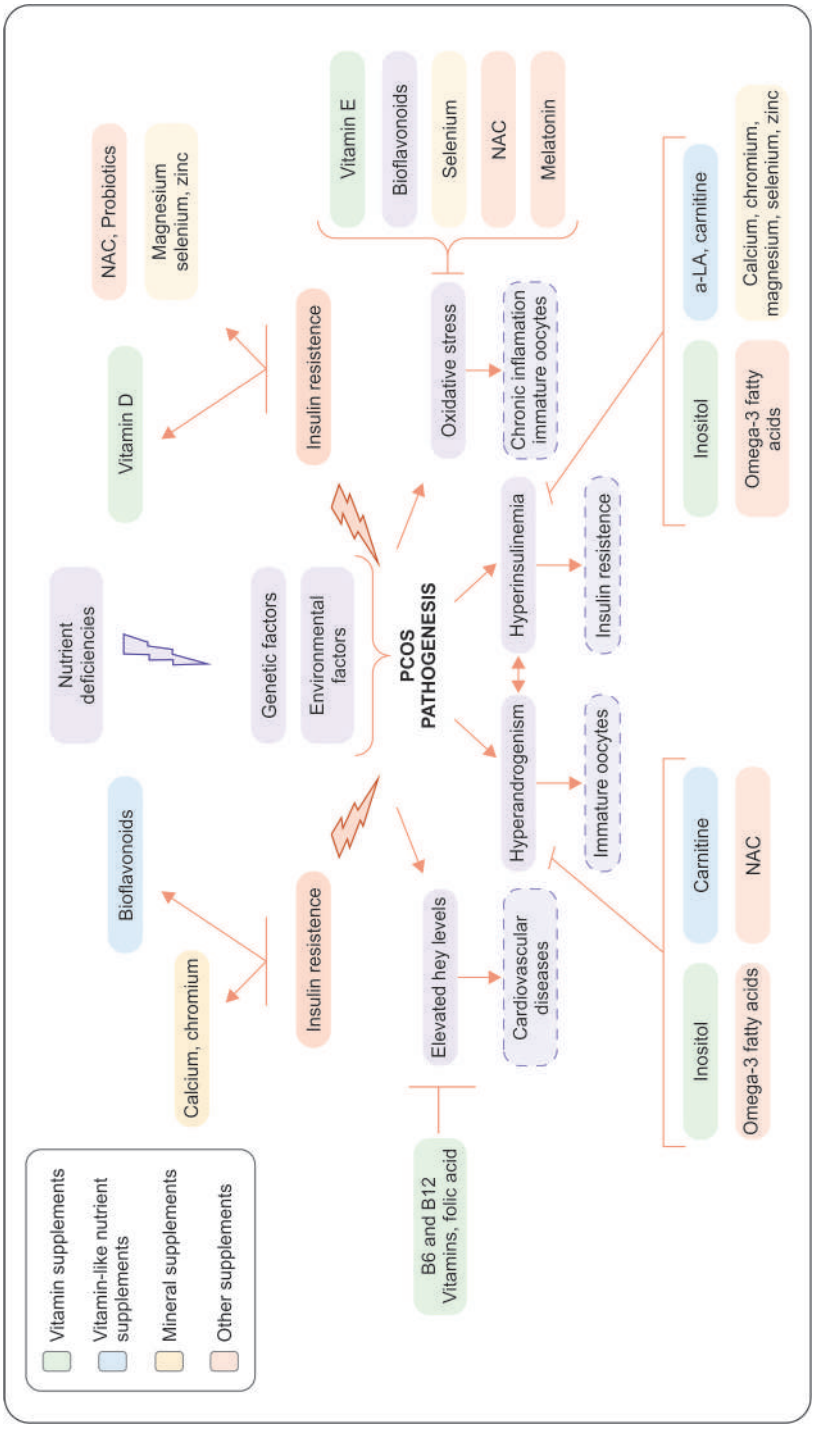


Fig. 1: Role of micronutrients and nutritional deficiencies in pathogenesis of PCOS[13]

Combined administration of myoinositol + L-methyl-folate is effective in PCOS, especially for overweight/obese patients with marked insulin resistance. Folate supplementation (5 mg/day) for 8 weeks among women with PCOS had beneficial effects on metabolic profiles. Three months of folic acid supplementation (1 mg/day) reduced the level of homocysteine in hyper-homocysteinemic women with PCOS. Therefore, the level of folic acid should always be kept high with the help of supplements.

Vitamin B12 (Cobalamin)

Insulin resistance, obesity, and elevated homocysteine were associated with lower serum vitamin B12 concentrations in PCOS patients.[9] Pernicious anemia is one of the causes of infertility and pregnancy occurred after supplementation with vitamin B12.[10] Cyanocobalamin helps in prevention of Neural Tube Defects.[11]

Vitamin B6 (Pyridoxine)

A positive correlation exists between insulin resistance (IR) and homocysteine (Hcy) levels vitamin B6 has been shown to improve conception rate as well as to treat premenstrual symptoms, especially where depression and anxiety were concerned. Pyridoxine supplementation improves conception rate.[12]

Vitamin B6 has a harmonizing effect on two more vital neurotransmitters –5-hydroxytryptamine and dopamine.

L-Arginine

Impaired arginine metabolism coupled to a defective Redox Conduit contributes to low plasma Nitric Oxide in Polycystic Ovary Syndrome. L-arginine plays a key role in pregnancy and fetal development. L-arginine improves circulation to reproductive system, especially endometrial and follicular blood flow, as shown by Doppler studies, by vasodilatory effect of nitric oxide. Nitric oxide donors improve the ovulation and pregnancy rates in anovulatory women with polycystic ovary syndrome treated with clomiphene citrate.[14] It improves the ovarian response, oocyte development, ovulation, fertilization rate, endometrial receptivity, implantation of embryo and thus pregnancy rates in anovulatory women with PCOS. Oral L-arginine supplementation in poor responder patients may improve ovarian response, endometrial receptivity, and pregnancy rate.[15]

Chromium

Infertile women with PCOS, who were candidates for IVF benefited from chromium supplementation for 8 weeks in terms of lowering hs-CRP and

improving gene expression. Chromium supplementation improves insulin resistance and ovarian and menstrual cyclicity in women with polycystic ovary syndrome. It increases the rate of developing regular menstruation by almost twofold after 5 months in PCOS women. It improves insulin sensitivity at the insulin receptor level, which reduces the Insulin Resistance and the obesity seen in PCOS.[16]

Zinc

It is required for eggs to reach maturity & be ready for fertilization, sexual development, ovulation, and the menstrual cycle.[17] Inadequate zinc levels could not stimulate tyrosine kinase in insulin receptor in PCOS patients. Zinc levels can play an important role in the development of IR in PCOS.

Magnesium

It is required for egg maturity and fertilization. Significantly lower concentration of serum magnesium was found in PCOS patients.[18]

Selenium

It prevents hypothyroidism during pregnancy.[19] It prevents accumulation of free radicals, recurrent early miscarriage, and unexplained infertility. Accumulation of free radicals in PCOS women due to insufficient selenium level leads to increased androgen levels including LH and total testosterone.

Vitamin E

Fertility benefits include improvement in epithelial growth in blood vessels and in the endometrium.[20]

Iron

Necessary for egg quality and egg maturation, also improves endometrial receptivity.

Nicotinamide

Nicotinic acid has a role in dyslipidemia involvement in the development of polycystic ovary syndrome. It can improve the lipid profile by lowering LDL-C particles and increasing HDL-C in the serum of PCOS patients. Niacin improves postprandial hyperlipidemia and cardiovascular risks indices via its lipid lowering as well as via pleiotropic effects in patients with PCOS.[21] Pharmacological elevation of NAD^+ may be an effective, noninvasive strategy for restoring and maintaining female fertility during ageing, and for improving the success of IVF.

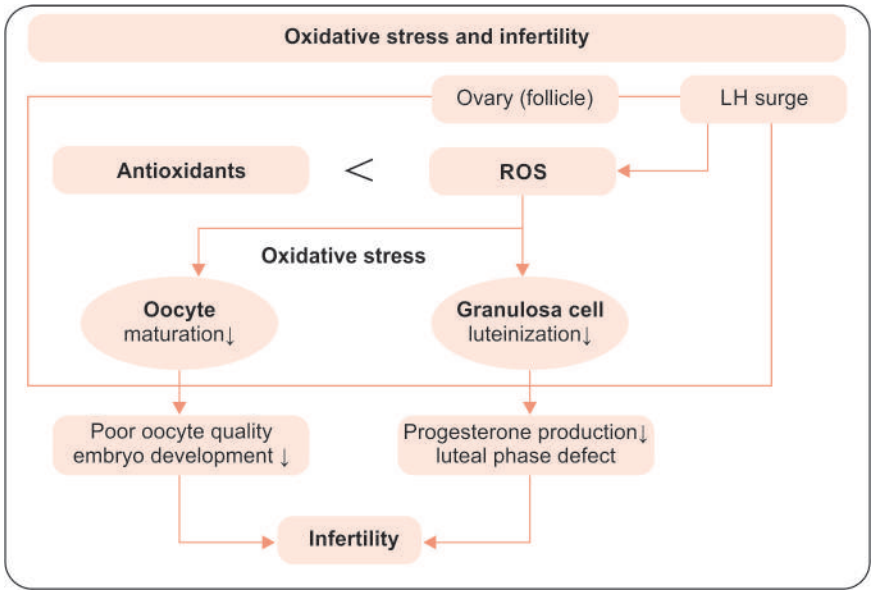
Inositols

It improves follicular maturation, ovulation rate, oocyte quality, nuclear and cytoplasmic oocyte development, and embryo quality. It improves insulin sensitivity, increases intracellular glucose utilization and plasma sex hormone binding globulin, reduces high insulin level, gestational diabetes, serum androgen concentration, and testosterone. It restores menstrual cycle. Myo-inositol (MI) thus helps in improving ovarian function and decreases hyperandrogenism and insulin.[22] It plays a pivotal role in the physiology of reproduction, and has beneficial effects on the development of oocytes, spermatozoa, and embryos.

Oxidative Stress and PCOS

Female dietary antioxidant intake and time to pregnancy among couples treated for infertility has shown direct relation between the two. Imbalance of reactive oxygen species has a clear link to female infertility. As explained in **Flowchart 1**, increased level of ROS in the follicular fluid hampers oocyte maturation and thus yields oocytes of poor quality. Increased ROS also takes place due to hyperglycemia in PCOS cases. It induces insulin resistance and hyperandrogenism in PCOS. Increased oxidative stress increases risks of cardiovascular disease in PCOS, hypertension, central obesity, and dyslipidemia.

Flowchart 1: Influence of oxidative stress on oocyte quality and female infertility[23]



Cotreatment of antioxidants and vitamins has positive effects on management of infertility. Female dietary antioxidant intake reduces time to pregnancy among couples treated for unexplained infertility. Up to 50–60% of recurrent pregnancy loss are attributable to oxidative stress. Decrease of antioxidants leads to increase of oxidation products contributing to PCOS.

Coenzyme Q 10 and Vitamin E

Antioxidant supplementation may be effective in controling the production of ROS and continues to be explored as a potential strategy to overcome reproductive disorders associated with infertility. Coenzyme Q 10 and vitamin E for 8 weeks in patients with PCOS provides improvement in SHBG concentrations. Antioxidants such as vitamin C & vitamin E, β carotene achieve an adequate anti-oxidant defense system and reduce the harmful effects of excess of oxidative stress. It has been shown that coenzyme Q 10 acts as an antioxidant which regulates steroidogenic enzyme functions dependent on cytochrome P450. It has been demonstrated that decreased level of β carotene may lead to the inactivation of P450 steroidogenesis in luteal cells.[24]

Up to 50–60% of recurrent pregnancy loss may be attributable to oxidative stress. Observational studies have confirmed a link between antioxidant-poor diet and recurrent pregnancy loss.

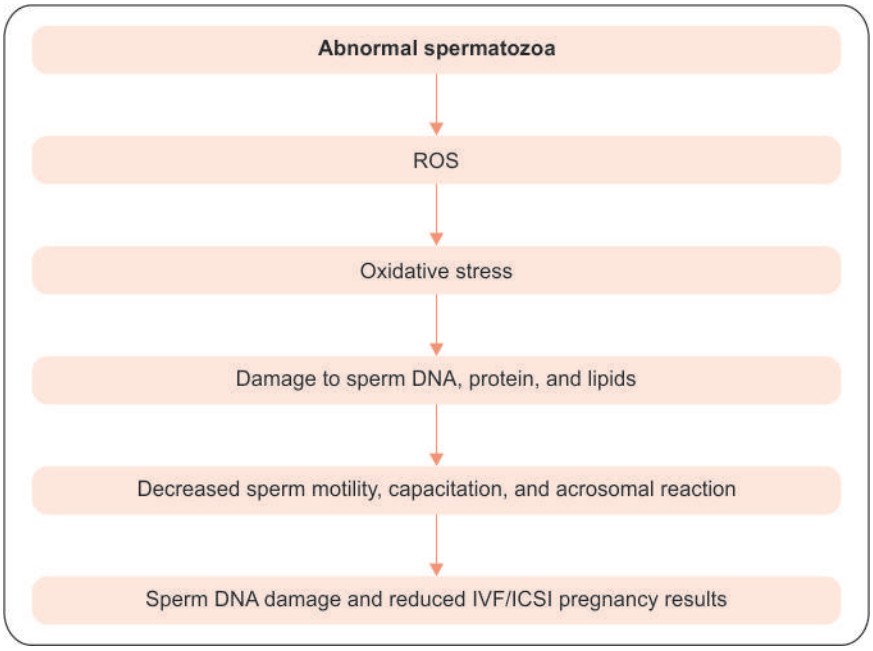
Male Infertility

Oxidative stress is detected in the semen of 44–80% of the infertile men. The direct impact of increased oxidative stress on sperm quality and thus poorer reproductive outcome is depicted in **Flowchart 2**.

DNA damage can be DNA fragmentation, mitochondrial DNA damage, telomere shortening, epigenetic abnormalities, or Y chromosome microdeletion. DNA Fragmentation Index (DFI) of >30% may result in male infertility, recurrent miscarriage, and poorer pregnancy rate.[25] **Figure 2** explains that pregnancy rate is inversely proportional to DFI percentage.

Sperm DNA damage has a negative effect on IVF/ICSI results too. Antioxidants protect against the effects of ROS on sperm DNA fragmentation. Antioxidants improve mitochondrial transport system, and increase enzymatic antioxidant activity. The role of each micronutrient and its positive role in improving male fertility is shown in **Table 1**. Thus when given at least for 3 months, it improve semen parameters in idiopathic infertility, neutralize the ROS, decrease the sperm DNA fragmentation and decrease seminal oxidative stress, improve pregnancy rate, and LBR.[26]

Flowchart 2: Influence of oxidative stress on sperm quality and male infertility[27]



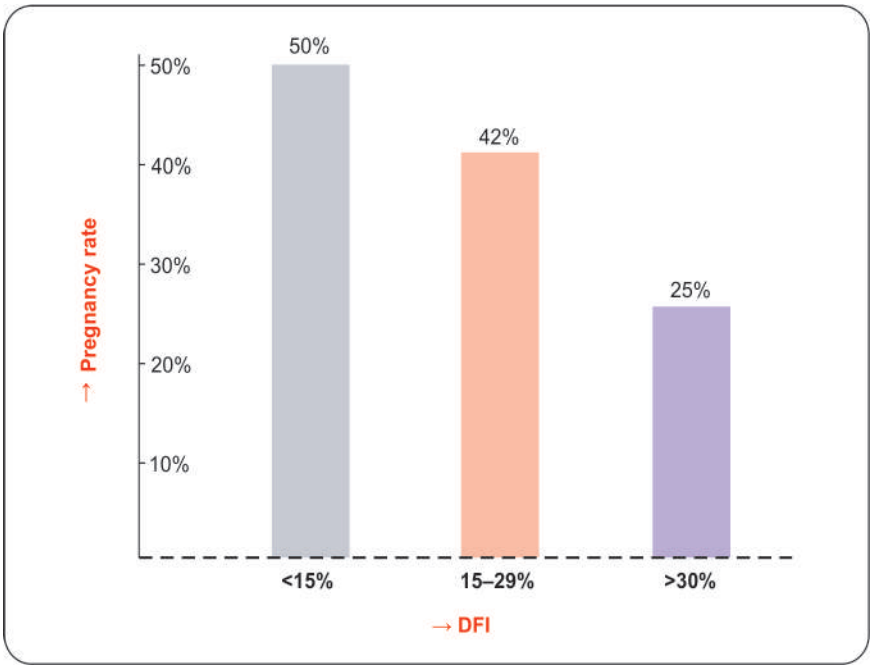


Fig. 2: Inverse relationship between sperm DFI and pregnancy rate[28]

TABLE 1 **Various micronutrients and their mechanism of action on male infertility[29]**

Micronutrients, doses	*Action*
Lycopene 6 mgm	Improves DNA damage
Vitamin E 400 IU	Scavenges free radicals
Vitamin C 40–100 mg	Neutralizes free radicals
Zinc 15–25 mgm	Improves sperm motility
Selenium 25–40 µgm	Improves sperm morphology
Folate 0.5 mgm	Scavenges free radicals, improves oocyte maturation
Vitamin E 8 mgm	Neutralizes free radicals
Ubiquinol 100 mgm	Decreases oxidative stress of seminal plasma
Resveratrol 40 mgm	Improves sperm vitality
N Acetyl cysteine	Improves sperm motility
Carnitine	Improves chromatin structure and motility
L Arginine	Nitric oxide is intra and inter cellular modulator
Astaxanthin	Capacitation
Vitamin B12	Reduces homocysteine levels

Conclusion

Supplementation with micronutrients may be a good strategy to adopt in healthy couples trying to conceive and in those with fertility problems as the supplementation has shown increased and faster conceptions. When there is an imbalance of reactive oxygen species there may be an increase in DNA structural damage, as well as a link to both male and female infertility.

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Chapter 21

Epigenetics of Nutrition

Arati Shah, Sanjay Gupte

Introduction

Nutrigenomics is the study of effect of naturally occurring substances in the food on molecular expression of genetic material in each individual. Nutrigenetics aims to understand how the genetic makeup of an individual coordinates the response to diet. The aim is to obtain a better understanding of nutrient-gene interactions depending on a genotype.

Nutrigenomics is the science that helps us understand why some people respond differently to the same foods, beverages, & supplements they consume based on their genetics. We can make use of that information to develop personalized nutritional recommendations.

Two Sides of a Coin

Nutrigenomics and Nutrigenetics are two sides of a coin. On the one hand, we know that diet and constituents in our diet can up regulate or down regulate the expression of all kinds of genes; on the other, genes can affect how we utilize the food **(Fig. 1)**.

There are more subtleties. Diet can also cause "epigenetic" modifications to genes. Those are changes not to the actual sequence of the genes but modifications to their expression which can actually be inherited.

Epigenetics refers to the control of gene expression via mechanisms not directly related to the DNA coding sequence.[1] As a result, different cells in an organism, all with the same genome, will differ greatly in phenotypes.

Epigenetics is an inheritable phenomenon that affects gene expression without structural genetic changes. Epigenetic phenomena include DNA Methylation, Histone modifications, and Chromatin remodeling.

These phenomena mainly affect the chormatin by changing its spatial conformation. It can either be opened out, allowing the binding of the transcription factor (mRNA), or it can be compacted, preventing transcription factor binding. Depending on this, cellular processes will be either upregulated, or downregulated.

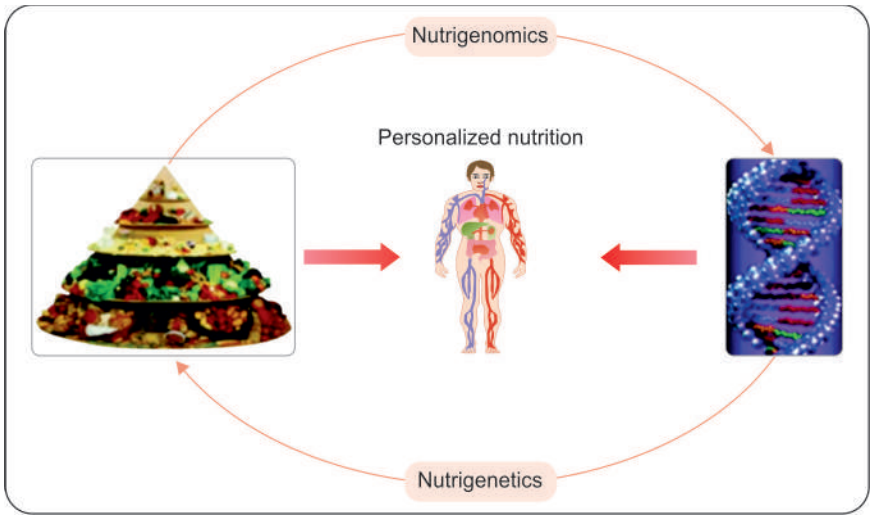

Fig. 1: Nutrigenomics and nutrigenetics

There are numerous other modifications too, of Chromatin structure that causes various epigenetic effects. Because epigenetic changes are reversible, this is now considered a crucial factor and has opened up a new field of nutritional intervention. During our lifetime, the nutrients we ingest can modify physiological as well as pathological processes through epigenetic mechanisms that are critical for gene expression as shown below.

- *Embryonic development:* Deficiency of folate, choline, protein restriction, or alcohol exposure can lead to DNA methylation in the fetus. In addition, folate deficiency also causes imprinting and protein restriction causes histone modifications.
- *Aging:* Folate deficiency causes DNA methylation. Calorie restriction leads to Histone acetylation.
- *Immune function:* Folate deficiency leads to DNA methylation.
- *Cancer:* Methyl-deficient diet causes Histone modification, microRNA formation. Genistein exposure leads to DNA methylation, microRNA formation. Curcumin causes microRNA formation.
- *Obesity, insulin resistance:* High-fat diet or methyl deficient diet leads to DNA methylation, microRNA. Curcumin causes Histone acetylation.
- *Inflammation:* Resveratrol causes Histone acetylation whereas AdoMet leads to Histone methylation.

Nutritional Epigenetics in Health and Disease

Nutrition is one of the most studied and better understood of many of the environmental epigenetic factors. Associations have been observed

between adverse prenatal nutritional conditions, postnatal health, and increased risk of disease. For instance, at its extreme, the Dutch Famine Birth Cohort resulting from the Dutch Famine of 1944–1945 has been used to study the effects of starvation during pregnancy and subsequent health and developmental outcomes including, but not limited to, increased risk of type II diabetes mellitus, cardiovascular disease, metabolic disorders, and decreased cognitive function in later life.[2-4]

The first months of pregnancy seem to have the greatest effect on disease risk. The women who faced famine in early pregnancy gave birth to normal size infant but offspring of these children were borne as small for gestational age, while women who faced famine during last two trimesters gave birth to small for date infants, but their offspring were of normal size. Simple nutritional intervention shows such a huge change. It seems likely that the fetus epigenetically adapts in response to a limited supply of nutrients. In humans, persistent epigenetic differences associated with prenatal exposure to famine have been ascribed to a lower degree of methylation of a gene implicated in insulin metabolism than their unexposed siblings.[5]

Nutrition in early life induces long-term changes in DNA methylation that impact on individual health and age-related diseases throughout life.[6,7]

Nutrients can either act directly by inhibiting epigenetic enzymes such as DNMT, HDAC, or HAT which are responsible for methylation or acetylation or by altering the availability of substrate necessary for those enzymatic reactions. This in turn modifies the expression of critical genes and impacts on our overall health and longevity.

A number of studies have reported the epigenetic effects of diet on phenotype and susceptibility to diseases throughout life. Folate metabolism is linked to phenotypic changes through DNA methylation, as folate, a water-soluble B vitamin, is a source of one-carbon for the synthesis of AdoMet, which is necessary for DNA methylation.[7-9]

Other methyl donor nutrients such as choline can also alter the DNA methylation status and subsequently impact gene expression.[8] It is thus important that during early pregnancy a mother receives a methyl donor nutrient rich diet to ensure correct fetal development. Imbalances at this early stage have shown to cause increased susceptibility to diseases as well as cancers not just in childhood, but through adulthood as well.

In a good example of nutrition affecting the gene expression, the experiments on mice with agouti genes are quite famous. Agouti gene is an obesity gene in the mouse when present it makes the mice very obese with brown fur. When these mice are fed with proper nutrients like folic acid, Choline, and Vit B12, the agouti variant of gene is silenced, and hence the pups are normal with normal weight and black fur like any other mice. In this case, maternal nutrient supplementation counteracted the negative effects of

chemical exposure, underscoring the importance of a good diet rich in fruit and vegetables and other high-quality foods.

Another striking example of the effects of early diets on epigenetics with consequences on the phenotype can be found in honey bees. The sterile worker bee differentiates from the fertile queen depending on the larval diet through epigenetic changes in DNA methylation patterns. Larvae designated to become queens are fed exclusively with royal jelly, which contains epigenetically active ingredients that silences a key gene which itself silences a group of queen genes.[8]

Nutritional Epigenetics and Cancer

The maintenance of DNA methylation patterns and DNA metabolism is largely dependent on nutrients, of which vitamin B12 and Folic acid are of prominence as epigenetically active ingredients. In one in vivo study, dietary folate intake was positively correlated with p16 tumor suppressor gene expression, a critical cancer-associated gene with frequent silencing DNA methylation of its promoter.[8] Low folate intake has been associated with hypomethylation and an increased risk of colorectal and pancreatic cancers.[10,11]

Going further, genes can also influence the foods that we select. There are studies which have looked at how genes affect various ingestion behaviors; for example, why some people tend to consume more sugar than others.

Researchers have identified a variation in a glucose transporter gene that is expressed in regions of the brain that regulate appetite. Variations of these genes is called glucose transporter type 2 is associated with an impaired glucose sensing ability. These people tend to consume more sugars on a daily basis.

There is also a gene which codes for a sweet taste receptor (Sweet Tooth!).

So some people tend to over consume sugar, based on impaired glucose sensing in the brain. Others tend to over consume sugar based on just their enhanced sweet taste perception on the surface of the tongue. In personalizing the advice; it's important for us to understand why some people have certain likes and dislikes to certain foods and try to understand some of those genetic drivers for some of those behaviors.

Similarly it is interesting to study why people respond differently to the same nutritional factors.

For example—some dieticians advice frequent small feeds to reduce weight while others profess only two meals a day, to be finished in 55 minutes without calorie restriction. There are people who have achieved weight loss with either one of these diets and vouch for the same. This difference is basically because of the gene variants in themselves. If we trace the path from

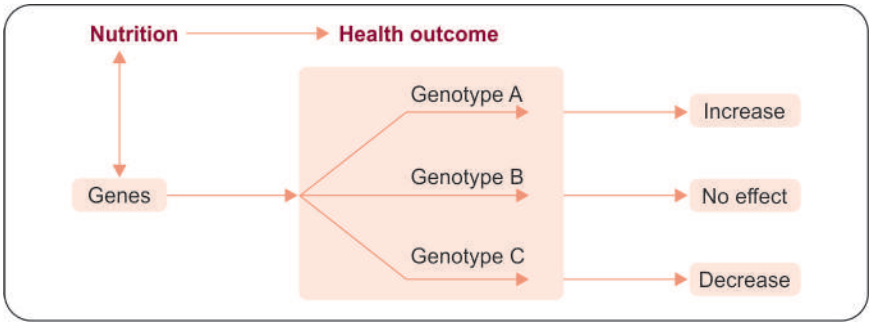

Fig. 2: Relationship of nutrition, genes and health outcome

virtually any nutritional factor to any health outcome when there are enough observational studies; we tend to see this heterogeneity of response. So we've all heard one day, fiber lowers the risk of colon cancer, another day you hear about a study that it has no effect and yet another where it might actually increase the risk. Well, that's true for virtually every nutritional factor.

It is important to know the genetics to see the effects of nutrition because the genetics of the population that's being studied matters.

There will be at least three different genetic situations.

Concept of "One size fits all" just no longer applies as far as diet advice is concerned because it will depend on the genotype of the person as shown in **Figure 2**.

When it comes to nutrigenomics, cooking can also make a difference!

Not only type of nutrients or food but how you cook it can make a difference, due to our genes. When we cook meat at high temperature—fish, chicken, red meat, or anything made of protein; if cooked at really high temperature like frying or grilling in a barbeque, the amino acids in those proteins interact with carnitine and sugar and form heterocyclic amines. Heterocyclic amines can form carcinogens in the body. This has been proven beyond doubt in animal models.

But as a human we have an advantage. We have a gene that can inactivate these heterocyclic amines. It's called NAT gene. It can inactivate these heterocyclic amines by adding a compound on to it called n-acetyl group. But if you have polymorphism where this NAT gene is modified; you may get cancer of the colon. So the bottom line is, if you have these gene polymorphisms, you're better off baking your fish and chicken, and not barbecuing or frying.

There are many other interesting genes which affect our diet performance and response.

Genetic make-up and dietary intakes are associated with alterations in waist circumference.

TABLE 1 **Waist circumference reduction**

Gene	*Variant*	*Interpretation*
MC4R	T	This genotype is associated with reduction in waist circumference

TABLE 2 **Body mass index**

Gene	*Variant*	*Interpretation*
FTO	T	This genotype is associated with normal BMI

TABLE 3 **Fat loss ability**

Gene	*Variant*	*Interpretation*
GSTP1	A	This genotype is associated with lower improvement in FFM (Fat free mass)

TABLE 4 **Fat intake**

Gene	*Variant*	*Interpretation*
BDNF	G/A	

MC4R is commonly known as the obesity gene **(Table 1)**. Mutations associated with it are excessive hunger, food seeking behavior, and hyperphagia. Its mutation carriers exhibit a significantly higher prevalence of binge eating disorder (BED) or loss of control eating. Mutation in MC4R gene account for 6–8% of obesity cases.

- Effect on BMI—proper weight loss ability of the body helps maintain a normal BMI and helps reduce waist circumference.
- FTO gene expression has been shown to be upregulated in the hypothalamus of the brain after food deprivation, which is associated with increased consumption of high calorie foods **(Table 2)**.
- Fat loss ability—a healthy diet comprising of MUFA and PUFA fats help enhancing weight loss and improves fat free mass after training **(Table 3)**.
- GSTP1 gene is responsible for improved endurance in exercises such as running and extensive physical training.

BDNF is also known as exercise motivation gene **(Table 4)**. It is associated with the synthesis of brain derived neurotrophic factor, an enzyme that acts on neurons of the CNS and peripheral nervous system. It regulates levels of motivation toward exercise and suppresses food intake.

Conclusion

We can conclude that nutrition can make tremendous difference in gene expression which in turn not only affects our health but also that of the generations to come. So the DNA based dietary advice results in greater understanding of recommendations, greater interest in updating one's knowledge and stronger motivation to change one's eating habits.

This should make the study of nutrigenomics and nutrigenetics really exciting for us as obstetricians dealing with the mother and the child, because we are in unique position to improve both gestational and post-gestational outcome.

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Appendix

FIGO
International Federation of Gynecology and Obstetrics
the Global Voice for Women's Health

FIGO nutrition checklist for pre-pregnant/early pregnant women

Good nutrition in the mother, both before and during pregnancy, is important in ensuring healthy outcomes for her and her baby. This checklist is designed for women to complete in conjunction with her health care professional in order to assess whether nutritional intake is sufficient, and provide a basis for the health care professional to advise where changes need to be made (if applicable).

For the woman to complete in conjunction with her healthcare professional:

1). Do you have any special dietary requirements (e.g. vegetarian, vegan, allergies)? If yes, please list below:

.....

.....

2). What is your:

a. Weight ..... kgs

b. Height ..... m

c. (Health care professional to complete): Divide weight in kg by height in metres then divide the answer by your height again to get your BMI.

Your BMI is ..... kg/m^2

3). Quality of diet

i) Do you eat meat or chicken 2-3 times per week? **Yes / No**

ii) Do you regularly eat more than 2 – 3 portions of fruit or vegetables per day? **Yes / No**

iii) Do you eat fish at least 1-2 times per week? **Yes / No**

iv) Do you consume dairy products (such as milk, cheese, yogurt) every day? **Yes / No**

v) Do you eat whole grain carbohydrate foods (brown bread, brown pasta, brown rice or other) at least once a day? **Yes / No**

vi) Do you consume packaged snacks, cakes, pastries or sugar-sweetened drinks less than 5 times a week? **Yes / No**

4).What is your:

i) If you are pregnant, did/do you take folate/folic acid supplements in pre-pregnancy and in early pregnancy (first 12 weeks)? **Yes / No**

ii) Do you get regular exposure to the sun (face, arms and hands for at least 10-15 mins per day)? **Yes / No**

iii) Has the doctor/nurse tested your haemoglobin (level of iron in the blood)? **Yes / No**

(Health care professional to complete) If yes, is it more than 110 g/l? **Yes / No** Enter the value: .....

If you have answered No to any of the questions in section 3 or 4 your nutritional status may need to be assessed in more detail.

Additional details for health care provider:

The intention is that this document will be adapted to the context of the country in which it is being used.

1. A healthy BMI is usually considered to be between 18.5–25 Kg/m^2, although this depends on age and geographical region.

2. For women who are not pregnant, counsel on achieving a healthy weight before conceiving.

* For pregnant women provide indications for appropriate gestational weight gain according to pregravidic BMI (see right). This may vary according to local contexts.

Pre-pregnancy BMI category	Total weight gain (kg)	Rate of weight gain 2nd and 3rd trimester (kg/wk)
Underweight <18.5 kg/m^2	12.5 - 18	0.51 (0.44 – 0.58)
Normal weight 18.5-24.9 kg/m^2 weight	11.5 - 16	0.42 (0.35 – 0.50)
Overweight 25.0 – 29.9kg/m^2 weight	7-11.5	0.28 (0.23 – 0.33)
Obese >30kg/m^2	5-9	0.22 (0.17 – 0.27)

From 2009 Institute of Medicine guidelines on gestational weight gain: https://www.nationalacademies.org/hmd/~/media/Files/Report%20Files/2009/Weight-Gain-During-Pregnancy-Reexamining-the-Guidelines/Report%20Brief%20-%20Weight%20Gain%20During%20Pregnancy.pdf

3. Q 3. i. is to assess whether vitamin B12, iron and protein intake is sufficient.

4. Q 3. ii. is to assess whether intake of antioxidants, micronutrients and fibre is sufficient.

5. Q 3. iii. is to assess whether intake of omega 3 / omega 6 polyunsaturated fatty acids, vitamin D and iodine is sufficient.

6. Q 3. iv. if the patient answers No to this question, calcium supplementation should be considered.

7. Q 3. v. and vi. – if No, advice should be given to increase wholegrains and reduce processed sugar intake.

8. Q 4. i. if not taking a folate supplement suggest a folate supplement.

9. Q 4. ii. if the patient has little sun exposure or has dark skin, consider vitamin D supplementation.

10. Q 4. Iii. if Hb < 110 g/l suggest an iron supplement. This cutoff may vary according to local contexts.

11. Health care professionals should consider any foods available in their country which are considered unsafe for pregnancy.

12. As well as the questions in the questionnaire, health care professionals should assess whether any other potential unsafe aspects of the woman's lifestyle should be counselled on, such as smoking, alcohol, recreational drug use, or lack of physical exercise

Pre-pregnancy – when planning a pregnancy

Involved professionals	Assessment considerations	Discussion points
• Community health workers • Nutritionists • Family doctors (GPs) • Ob-gyns • Midwives	• Diet composition • Physical activity history • Height, weight, BMI • Obesity risk - WC (+ other anthropometric measures) • Anemia • Risk of specific nutritional problems (low nutrient density) - Folate - Iron - Calcium - Vitamin B12 - Vitamin D - Iodine - Zinc - PUFAs	• Importance of a healthy diet and exercise • Problems of sedentary behaviour such as screen-time • Risky behaviors and exposures - Tobacco, alcohol recreational drugs - Environmental toxins • Chronic disease screening and management • Supplementation - Folic acid supplementation 400 µ/day - Other nutrients (iron, iodine, vitamin B12)

During pregnancy

Involved professionals	Assessment considerations	Discussion points
• Community health workers • Nutritionists • Family doctors (GPs) • Ob-gyns • Midwives	• Diet composition • Physical activity history • Height, weight, BMI, WC (other anthropometric measures?); • Gestational weight gain • Blood pressure • Risk of specific nutritional problems (low nutrient density), deficiencies from specific diets or under-nutrition) *First trimester* - Folate - Vitamin B12 - Iodine - PUFAs *Second and third trimesters* - Iron, iodine, zinc, copper, calcium - Folate, B vitamins, vitamin D - Energy (+450 kcal/day) - Iodine - PUFAs	• Dietary counselling • Safe levels of exercise • Sedentary time • Weight management and gestational weight gain • Risky behaviors and exposures - Tobacco, alcohol recreational drugs - Sources of food borne infection • Pregnancy complication screening and management (GDM, blood pressure) • Supplementation - Folic acid supplementation 400 µ/day - Iron supplementation 30-60 mg/day - Other nutrients as required (iodine, vitamin B12, vitamin D)

This document, including the above table, is based upon The International Federation of Gynecology and Obstetrics recommendations on adolescent, preconception, and maternal nutrition: "Think Nutrition First", Hanson M et al, 2015, which can be accessed at http://obgyn.onlinelibrary.wiley.com/hub/issue/10.1002/(ISSN)2055-7191(2015)54/

FIGO is a non-governmental organisation specialising in ensuring improvement in women's health around the world. It is the only global organisation representing national societies of obstetricians and gynecologists, and works together with other medical professionals and organisations to ensure the best possible health for the women of the world.

TABLE 1 **FIGO recommendations on adolescent, preconception, and maternal nutrition: Action points for health-care providers**

Pre-pregnancy – adolescent girls		
Involved professionals	***Assessment considerations***	***Discussion points***
• School health educators • Community health workers • Nutritionists • Family doctors (GPs) • Ob-gyns	• Diet composition • Physical activity • Height, weight, BMI • Obesity risk – Waist circumference + other anthropometric measures • Anemia • Risk of specific nutritional problems (low nutrient density) – Folate – Iron – Calcium – Vitamin B12 – Vitamin D – Iodine – Zinc – PUFAs	• Importance of a healthy diet and exercise • Problems of sedentary behavior such as screen time[a] • Weight loss counseling • Risky behaviors and exposures • Pregnancy risk – Contraception (timing and spacing) – encourage reversible methods such as IUD and implants that do not require regular action – Folic acid supplementation 400 µg/day – Encourage early pregnancy care • Local environmental issues (e.g., pollution, chemicals)

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Pre-pregnancy – when planning a pregnancy		
Involved professionals	***Assessment considerations***	***Discussion points***
• Community health workers • Nutritionists • Family doctors (GPs) • Ob-gyns • Midwives	• Diet composition • Physical activity history • Height, weight, BMI • Obesity risk – Waist circumference + other anthropometric measures • Anemia • Risk of specific nutritional problems (low nutrient density) – Folate – Iron – Calcium – Vitamin B12 – Vitamin D – Iodine – Zinc – PUFAs	• Importance of a healthy diet and exercise • Problems of sedentary behavior such as screen time • Weight loss counseling • Risky behaviors and exposures – Tobacco, alcohol, recreational drugs – Environmental toxins • Chronic disease screening and management • Supplementation – Folic acid supplementation 400 µg/day – Other nutrients as required (iron, iodine, vitamin B12)

Contd...

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During pregnancy		
Involved professionals	***Assessment considerations***	***Discussion points***
• Community health workers • Nutritionists • Family doctors (GPs) • Ob-gyns • Midwives	• Diet composition • Physical activity • Height, weight, BMI, waist circumference (other anthropometric measures?) • Gestational weight gain • Blood pressure • Gestational diabetes risk • Anemia • Risk of specific nutritional problems (low nutrient density, deficiencies from specific diets or undernutrition) First trimester – Folate – Vitamin B12 – Iodine – PUFAs Second and third trimesters – Iron, iodine, zinc, copper, calcium – Folate, B vitamins, vitamin D – Energy (+450 kcal/day)	• Dietary counseling • Safe levels of exercise • Sedentary time • Weight management and gestational weight gain • Risky behaviors and exposures – Tobacco, alcohol, recreational drugs – Sources of food-borne infection – Environmental toxins • Pregnancy complication screening and management (GDM, blood pressure) • Supplementation – Folic acid supplementation 400 µg/day – Iron supplementation 30–60 mg/day – Other nutrients as required (iodine, vitamin B12, vitamin D)

Contd...

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Post-pregnancy (during lactation)		
Involved professionals	***Assessment considerations***	***Discussion points***
• Community health workers • Nutritionists • GPs • Ob-gyns • Midwives • Pediatricians • Lactation consultants	• Diet composition • Risk of specific nutritional problems (low nutrient density) – Protein – PUFAs – Vitamins/minerals – Energy (additional intake as recommended by each country; approximately +330 kcal/day) • Weight status and postpartum weight loss • Screening for diabetes as appropriate • Breastfeeding success	• Healthy diet and physical activity, sedentary time • Achieving a healthy weight • Appropriate supplementation – iron and folic acid are recommended during first 3 months after delivery • Breastfeeding support • Nutritious weaning foods • Interpregnancy spacing and contraception • Chronic disease screening and management (type 2 diabetes, blood pressure)

Abbreviations: IUD, intrauterine device; BMI, body mass index; GPs, general practitioners; PUFAs, polyunsaturated fatty acids; GDM, gestational diabetes mellitus.

[a] Time spent on computers, video games, and watching television.

TABLE 2 **FIGO recommendations on adolescent, preconception, and maternal nutrition: Specific nutritional requirements before conception, and increases for pregnancy and lactation, based on Institute of Medicine recommended dietary allowance and adequate intake guidelines.[a]**

Nutrient	*Daily intake requirement*			*Function*	*Food sources*	*Risk factors for deficiency/consideration for supplementation*
	Pre-pregnant	*Pregnant*	*Lactating*			
Protein	60 g	71 g		Building blocks for structural and functional components of cells	Meat, poultry, fish, eggs, dairy products, legumes, grains, nuts, seeds	Protein energy malnutrition
Omega-6 PUFAs	11–12 g	13 g	13 g	Component of structural membrane lipids, involved in cell signaling, precursor of eicosanoids	Nuts, seeds, vegetable oils (corn, sunflower, soybean). For arachidonic acid: poultry, eggs, fish	Fat intake mainly from saturated fat sources
Omega-3 PUFAs	1.1 g	1.4 g	1.3 g	Neurological development, growth, precursor of eicosanoids	Fish oils, fatty fish, flaxseed oil, nuts (e.g., walnuts)	Low intake of fatty fish, fat intake from saturated fat sources
Carbohydrates	130 g	175 g	210 g	Fuel for growth	Starchy vegetables, grains, sugars	Protein energy malnutrition

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Nutrient	Daily intake requirement			Function	Food sources	Risk factors for deficiency/consideration for supplementation
	Pre-pregnant	Pregnant	Lactating			
Folate	400 µg	400–600 µg	600 µg	Neurological function, erythropoiesis, neural tube formation, brain development	Liver[b], yeast extract, green leafy vegetables, legumes, citrus fruits, fortified breakfast cereals	Family history of neural tube defects, low folate diet[c]
Vitamin B12	2.4 µg	2.6 µg	2.8 µg	Neurological function, erythropoiesis, neural tube formation, brain development	Milk/dairy products, meat (especially liver[b]), poultry, fish, and eggs	Vegan/vegetarian diets, malabsorption disorders, communities where undernutrition is prevalent
Vitamin A (as retinol activity equivalents)	700 µg	750–770 µg	1300 µg	Vision, immunity, growth, organ and limb development, red blood cell production	Yellow and orange vegetables, cod liver oil, eggs, dairy (sources of vitamin A precursors: carotenoids)	Endemic in some areas. Zinc deficiency may interfere with vitamin A metabolism
Vitamin D	≥600 IU[d]	≥600 IU[d]	≥600 IU[d]	Immune function, bone growth, calcium and phosphorus balance, insulin secretion, blood pressure regulation	Fatty fish, eggs, dairy	Limited sun exposure, low dietary intake, obesity

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Nutrient	Daily intake requirement			Function	Food sources	Risk factors for deficiency/consideration for supplementation
	Pre-pregnant	Pregnant	Lactating			
Vitamin B6	1.3 mg	1.9 mg	2.0 mg	Multiple enzyme function – protein metabolism, neurological function	Poultry, fish (especially tuna), meats, legumes, potatoes and other starchy vegetables, noncitrus fruits, nuts, and seeds	Alcoholism, poor diet, systemic inflammation
Iodine	150 µg	220 µg	290 mg	Thyroid adaptation to pregnancy, brain development	Seaweed, seafoods, iodized salt	Endemic iodine deficiency due to low soil content
Iron	15–18 mg	27 mg	9 mg	Hemoglobin synthesis, organ function	Meat, poultry, fish, seafood, molasses, prunes, lentils, kidney beans, yeast extract, tofu, cashew nuts	Malaria infection/endemic area[e], vegetarian diet, malnutrition
Calcium[f]	1000–1300 mg	1000–1300 mg	1000–1300 mg	Muscle function, skeletal development, nerve impulse transmission, hormone secretion	Dairy products, tofu, sardines, beans, Chinese cabbage, oranges, figs, kale, broccoli	Low intake of dairy products; vegan diet, adolescent growth spurt

Contd...

Contd...

Nutrient	Daily intake requirement			Function	Food sources	Risk factors for deficiency/consideration for supplementation
	Pre-pregnant	Pregnant	Lactating			
Selenium	55 µg	60 µg	70 µg	Fertility, fetal growth, prevention of oxidative stress	Plant foods (e.g., wheat) grown in selenium-rich soil; animals fed on selenium-rich plant foods	Low regional soil selenium content
Zinc[f]	8–9 mg	11–12 mg	12 mg	Immune function/ infection resistance, growth, neurodevelopment	Oysters, other shellfish, red meat, nuts legumes, poultry, eggs, seeds (sesame, pumpkin, sunflower)	Protein-energy malnutrition, diets low in animal protein and/or high in phytates (whole grains). Iron and calcium supplements decrease zinc absorption
Choline	400–425 mg	450 mg		Membrane function, nerve impulse transmission, brain development, neural tube formation	Liver[b], eggs, beef, fish, seafood, milk, wheat germ	Vegan/vegetarian diets

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Nutrient	Daily intake requirement			Function	Food sources	Risk factors for deficiency/consideration for supplementation
	Pre-pregnant	Pregnant	Lactating			
Biotin	25–30 µg	30 µg		Immune function, neurological function	Egg yolk, legumes (particularly soybeans and lentils), sunflower seeds, milk, cheese, chicken, pork, beef, and some fruits and vegetables	High consumption of egg whites
Copper	890–900 µg	1000 µg		Immune function, connective tissue formation, iron metabolism, central nervous system function	Organ meats, grains, shellfish (oysters), nuts, seeds, and cocoa products	Iron and zinc supplementation reduces copper absorption

[a] Source: Institute of Medicine [107,119,132,136,141].
[b] Liver is very high in vitamin A and high consumption is not recommended in the periconceptional period because it poses a teratogenic risk.
[c] Most women in the reproductive years should be supplemented with folate 400 µg/day to decrease the risk of neural tube defects, but attention should be paid to vitamin B12 status—excess folate from supplements may mask/exacerbate the effects of vitamin B12 deficiency.
[d] Intakes of between 1000 and 2000 IU/day are likely to be beneficial and not harmful.
[e] Malaria causes iron delocalization rather than deficiency, so supplementation may not be helpful unless malaria prophylaxis/treatment is used in conjunction.
[f] The intake range indicates adult versus adolescent requirements. Adolescents require the higher intake; adults the lower intake.

- FIGO calls for increased awareness of the impact of women's nutrition on themselves and future generations, and supports action to improve nutrition among adolescent girls and women of reproductive age.
- FIGO calls for greater attention to the links between poor maternal nutrition and NCDs in the next generation as a core component to meeting global health goals.
- FIGO calls for public health measures to improve nutrition education—particularly for adolescents—and access to preconception services for women of reproductive age to assist with planning and preparation for healthy pregnancies, emphasizing the importance of healthy nutrition.
- FIGO recommends that adolescent, preconception, and maternal nutrition should be part of a life course approach that views perinatal health within the context of women's overall health, and that of their partners, and dismisses the artificial dichotomy between reproductive and nonreproductive health.
- Standard care should involve a wide range of health-care providers working together, with a focus on nutrition, health, and lifestyle during adolescence and through a woman's reproductive life and beyond.
- FIGO recommends promotion of a varied and healthy diet as the first step to meeting the nutrient needs of adolescent girls and women, with the provision of supplements or fortified foods when necessary.
- FIGO emphasizes the importance of optimizing the nutritional status of adolescent girls and women and encouraging the adoption of good dietary and lifestyle habits before pregnancy.
- FIGO recommends that attention be paid to preconception body weight and BMI as modifiable risk factors with important effects on a woman's nutritional status:
  - Underweight women may be lacking in a number of important nutrients, and their diets should be carefully assessed and supplemented as required.
  - Overweight or obese women may have poor diets that are high in energy but low in nutritional value.
- FIGO recommends that micronutrient deficiencies are recognized and rectified through interventions, including dietary diversity, consumption of fortified foods, and supplementation as appropriate.
- FIGO strongly recommends that hazardous exposures and behaviors such as smoking, alcohol intake, or use of recreational drugs are avoided prior to conception, and definitely should be avoided in pregnancy because of the risk of detrimental effects on fetal nutrition, growth, and development.

- FIGO strongly recommends that pregnant women have early access to prenatal care to receive appropriate nutrition counseling and interventions, and treatment for conditions that jeopardize their pregnancy outcome, such as malaria, tuberculosis, HIV, gastrointestinal infections, and NCDs.
- FIGO recommends that health-care professionals take action to recommend and monitor appropriate gestational weight gain in relation to prepregnancy BMI. In resource-constrained settings, gestational weight gain monitoring should not occur at the expense of assessments such as blood pressure measurement, urine testing for protein, and abdominal examination.
- FIGO recommends that pregnant women exercise moderately for at least 30 minutes per day. Most women should increase their dietary energy intake by approximately 340–450 kcal per day during the second and third trimester. Extreme exercise or hard physical labor should be avoided during late pregnancy.
- FIGO calls for action to reduce exposure of adolescents and pregnant women to mercury, arsenic, lead, and cadmium, which can be ingested via food and water. These heavy metals can have detrimental effects on fetal growth and development.
- FIGO recommends that the period that follows birth is used to improve the nutritional status of both mother and child. FIGO endorses the WHO recommendation of exclusive breastfeeding for the first 6 months of the infant's life.
- FIGO supports the adoption of gender-sensitive policies to improve access to adequate and nutritious food for girls, adolescents, and women.
- FIGO makes specific recommendations to achieve this goal, and advocates concerted action by a range of stakeholders including donors and international organizations to enact them. FIGO maintains that THINKING NUTRITION FIRST should be a priority in all countries.

This is based upon The International Federation of Gynecology and Obstetrics recommendations on adolescent, preconception, and maternal nutrition: "Think Nutrition First," Hanson M et al, 2015, which can be accessed at http://obgyn.onlinelibrary.wiley.com/hub/issue/10.1002/ijgo.2015.131.issue-S4/

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NUTRITION IN WOMEN: ACROSS AGES

ISBN:XXX-XX-XXXXX-X-X

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