Review

Periconceptional Mediterranean diet during pregnancy on children's health

HAVVA ÇOBANOĞULLARI[1], MAHMUT CERKEZ ERGOREN[2], MUNIS DUNDAR[3], MATTEO BERTELLI[4,5,6], PINAR TULAY[2,7,*]

[1] Near East University, Faculty of Medicine, Department of Molecular Medicine, Nicosia, Cyprus; [2] Near East University, Faculty of Medicine, Department of Medical Genetics, Nicosia, Cyprus; [3] Erciyes University, Faculty of Medicine, Department of Medical Genetics, Kayseri, Turkey; [4] MAGISNAT, Peachtree Corners, USA; [5] MAGI Euregio, Bolzano, Italy; [6] MAGI'S LAB, Rovereto, Italy; [7] Near East University, DESAM Research Institute, Nicosia, Cyprus

Keywords

Congenital defects • Mediterranean diet • Periconceptional period • Pregnancy

Summary

During pregnancy, rapid and subtle physiological changes are observed from conception to birth. Nutrition and other lifestyle factors before and during pregnancy have been shown in the literature to influence the health of both mother and child. A healthy and varied diet during pregnancy can provide adequate energy and nutrients for both the mother and the growing fetus. Current research focuses on the periconceptional phase, which includes the early processes of gametogenesis, embryogenesis and placentation. A variety of abnormalities and pregnancy-related problems occur during this period, including congenital defects, fetal loss, miscarriage and preterm birth. A varied and balanced diet during periconception is important to maintain fetal development and growth. To date, numerous studies have been conducted to investigate the effects of consuming different nutrients, foods or food groups during pregnancy on the health of mother and child. For example, the Mediterranean diet is considered as a balanced, nutrient-rich diet due to the low consumption of meat products and fatty foods and the high consumption of vegetables, cheese, olive oil, fish, shellfish and little meat. While many studies have been conducted in the literature to investigate the effects of a Mediterranean diet during pregnancy on fetal health, the results have been inconclusive. The aim of this article is to review the current literature on the Mediterranean diet during pregnancy.

Introduction

Pregnancy has a complex nature involving growth, development and maturity processes. From fertilization to birth, a whole range of processes take place to prepare the fetus for life outside the womb [1]. Inherited diseases or chromosomal aberrations has been a central aspect of perinatal research and neonatal health. However, recent studies have been conducted to investigate the interaction between mother and fetus from different angles [2]. Pregnancy consists of two main periods including the embryonic period and the fetal period. The embryonic period lasts eight weeks, the foetal period lasts from the ninth week of pregnancy until birth [1, 3]. The first two weeks of the embryonic period are crucial because the embryo is extremely sensitive to an unfavourable environment (changed hormone concentrations, inadequate blood and nutrient supply), and in certain situations prenatal mortality may occur. From the second until the eigth week, the embryo is very sensitive to teratogenic drugs as embryonic development is initiated at this period. Finally, important physiological adaptations and less severe morphological changes occur during the fetal period. This period is critical due to changes that result in fetal programming that conditions the optimal or problematic organ systems affecting the whole organism [3, 4].

Some of the physiological changes that occur during pregnancy result in an increase in plasma volume and red blood cells, and a reduction in concentrations of nutrient-binding proteins and micronutrients that circulate in the body [5]. Dietary intake, limited exercise, smoking and alcohol use are critical to the health of women and their children during pregnancy and breastfeeding [6, 7]. Nutrition is considered one of the most critical environmental elements influencing embryo and foetal development and maternal health [8]. During pregnancy, the need for nutrients increases to support the growth and development of the fetus and to maintain maternal metabolism [9]. In recent years, several studies and comprehensive meta-analysis have shown that inadequate intake of important macronutrients and micronutrients can adversely affect pregnancy outcomes and neonatal health [9]. Deficiencies in micronutrients, in particular, have been linked to an increased risk of infertility, fetal structural abnormalities and long-term illnesses [8].

Since pregnancy is composed of different phases that continue, maternal nutrition and hormones have a significant influence on all phases of embryonic and foetal development, maternal nutrition and hormones have a significant impact on all stages of embryonic and fetal development [10]. Importantly, the periconceptional period is considered as a critical period for fetal development and health. During this period, a variety of

abnormalities and pregnancy-related problems occur, including congenital defects, fetal losses, miscarriages and preterm delivery [11]. According to the literature, periconceptional nutrition has an impact on fetal development and growth. It is important that the intake of certain nutrients during pregnancy, especially, the Mediterranean diet (MD) is considered a healthy and balanced diet. A number of studies have proven that it helps to prevent maternal and fetal diseases during pregnancy [11, 12].

Pregnancy and diet

Nutrition during pregnancy

Pregnancy is a 40-week period of life with different nutritional requirements for mother and child, and it is an important period of life for both. Pregnancy involves rapid and subtle physiological changes from conception to birth [7]. Diet and other lifestyle factors such as smoking and alcohol consumption before and during pregnancy and lactation have been shown to affect child health [13]. In addition, an unbalanced diet during pregnancy has been associated with serious pregnancy complications [14]. Although the role of nutrition in pregnancy has been investigated in several studies, the results have been inconclusive [15].

A healthy and varied diet during pregnancy can provide adequate energy and nutrients for both the mother and the growing fetus [5]. Several studies that investigated the effect of diet on pregnancy outcome focused on only one or a few nutrients [16]. High consumption of saturated fats, low consumption of polyunsaturated fats, carbohydrates and soft drinks, for example, have been associated with gestational diabetes mellitus (GDM) and hypertension [16]. In addition, calcium intake has been associated with a lower risk of preeclampsia and fewer preterm births [17]. Deficiencies in micronutrients such as folic acid, iron, and zinc and vitamins are common in pregnant women [18]. Low Fe consumption, for example, has been associated with anaemia, while low folate intake has been associated with neural tube abnormalities or preterm birth [7, 9]. Since vitamins and some minerals are important components of the immune system, deficiencies in these micronutrients can lead to harmful infections [8]. It is believed that micronutrient supplementation may be beneficial in preventing adverse pregnancy outcomes [19].

Extensive research has been conducted over the past decade to determine the relationship between intrauterine fetal development, postnatal phenotype programming and the risk of developing noncommunicable diseases including cardiovascular disease and neoplastic disease [20, 21]. An unfavourable nutritional status during pregnancy, namely reduced iodine, folic acid and protein intake, has been associated with intrauterine cerebellar development, altered cerebellar methylation patterns and higher lipoperoxidation in the children [22, 23]. In addition, consumption of fish and polyunsaturated fatty acids improved embryo morphology following *in vitro* fertilization (IVF) treatment [24]. Currently, research focuses on the periconceptional period which is 14 weeks before and up to 10 weeks after conception and includes the early processes of gametogenesis, embryogenesis, and placentation [25]. Researchers have reported that an unhealthy maternal lifestyle during periconception has negative effects on reproductive outcomes [7, 26]. Importantly, reproductive failures occur during the periconceptional period, i.e. implantation failure, early pregnancy loss, miscarriage, congenital malformations in newborns, and fetal growth failure [26]. Maternal periconceptional nutrition affects fetal programming, placental cognition and fetal and maternal competition for food [27]. In addition, diet can influence embryonic development through biochemical signals in the environment of uterus. It has been shown that optimal nutrition during periconception promotes fetal growth and development [15]. Studies in animals and humans have shown that epigenetic events expressed later in adulthood are related to early embryonic stages and the quality of maternal periconceptional nutrition [7].

Notably, maternal one-carbon (I-C) metabolism plays an important role in the DNA methylation patterns of the offspring that influence postnatal gene expression and disease progression [26]. One carbon metabolism is altered by environmental factors such as inadequate folate and folic acid intake, lifestyle and medication use as well as common polymorphisms such as the methylenetetrahydrofolate reductase (*MTHFR*) C677T polymorphism [26, 28]. Consequently, genetic and environmental varaibles influence I-C metabolism as well as intrauterine DNA methylation, gene expression and the transcriptome may explain the association between maternal environment and long-term outcomes [20, 26].

In summary, the health of every human being from conception to adulthood requires a varied and balanced diet. The developmental processes already take place during pregnancy and are influenced by the mother's diet. Therefore, nutrition should be planned in order to avoid unfavourable pregnancy consequences.

Mediterrranean diet in gestation

Fetal development depends on maternal nutritional and metabolic conditions. The baby's physiology and metabolism can be permanently altered and shaped by the intrauterine environment [29]. Several studies have investigated the association between the intake of various nutrients, foods or food groups during pregnancy and maternal and fetal diseases [30]. The Mediterranean diet, with its low intake of meat products and high-fat foods, is a balanced, nutritious diet that is considered a standard for diet quality because of its components such as vegetables, cheese, olive oil, fish, shellfish and little meat [31]. The health effects of this diet were described as early as the 1950s. The American scientist Ancel Keys was the first to note the effects of diet and lifestyle on cardiovascular disease [32].

The Mediterranean diet appears to provide adequate caloric and nutrient intake in appropriate amounts and proportions. It is distinguished by its high methyl donor content

for one-carbon metabolism, which is engaged in growth and programming activities, notably during the periconceptional period [33] Many studies have been undertaken to investigate the effect of Mediterranean diet on maternal health and offspring health. For instance, the Mediterranean diet is associated with a higher chance of clinical pregnancy and live birth after IVF, and a lower incidence of infertility [34, 35]. A significant study undertaken by Australian experts found that the Mediterranean diet protects against hypertensive problems during pregnancy (HDP) [36]. Similarly, other studies found that diets rich in vegetables and fruits were associated with pre-eclampsia and gestational hypertension [37, 38]. In contrast, a higher risk of preeclampsia was observed in women who adhered to a Western diet [38].

In another study, higher consumption of animal proteins before pregnancy was linked to an increased risk of gestational diabetes, whereas higher consumption of plant-based proteins was linked to a lower risk of metabolic disorders [39]. Furthermore, in a study carried out in Iran, where the consumption of fast food is very high, it was found that the consumption of chips in particular increased the risk of gestational diabetes [40]. Sibling studies have shown that those who were exposed to a diabetic environment in utero have a higher risk of developing diabetes, regardless of whether they have a genetic predisposition [41].

Moreover, other studies that have examined the effect of diet on neonatal and fetal development have shown that children of women who have a diet rich in vegetables and fruits have a lower risk of developing congenital limb defects [42]. Similarly, the risk of developing orofacial cleft is lower in offspring of women who have a periconceptional diet rich in fruits and vegetables [43]. In addition, a "one-carbon" diet high in fish and seafood has been associated with a lower incidence of congenital heart disease (CHD) and septal abnormalities [43, 44]. In a study, eating lean fish during periconceptional period has been associated with higher risk of low birth weight [45]. Finally, several studies have found that the Mediterranean diet reduces the risk of small gestational age (SGA) in newborns [46, 47].

Although the impact of the diet on the health of pregnant women and offspring have not been clearly established, the benefits of the Mediterranean diet for mothers, fetuses, and offspring are well documented. This diet should be promoted before, during, and after pregnancy.

Mediterranean-style diet and common health problems in pregnancy

Mediterranean diet and gestational diabetes and glucose intolerance

Gestational diabetes mellitus (GDM) is a glucose intolerance that occurs during pregnancy [48]. Depending on the diagnostic threshold and the population studied, 1-28% of all pregnancies are affected [49, 50]. GDM is associated with poorer pregnancy outcomes and a higher risk of maternal and child morbidity in the long term [51]. Age of the mother and a family history of type 2 diabetes and obesity are among the nonmodifiable risk factors associated with GDM [52]. GDM, in particular, type 2 diabetes (T2D) has a genetic component and aggregates in families. It has been demonstrated that women who have a diabetic sibling have an increased risk of developing GDM [53, 54]. Furthermore, identifying modifiable risk factors linked with GDM is critical for developing effective preventative approaches and avoiding negative health effects [55]. Several studies focused on dietary components during pregnancy as one of the modifiable factors contributing to GDM [56]. High sugar consumption, for example, is thought to contribute to an inflammatory process that may be associated with insulin resistance [57]. Although a number of studies have been undertaken to determine the link between dietary patterns and GDM, the results have been inconclusive [58, 59].

Two studies found that eating high amounts of dietary fibre has been linked to lower risk of GDM, but this finding is not confirmed by other studies [60]. The results of another study show that a high glycaemic load in the diet contributes to the development of GDM [61]. Interestingly, several studies have been conducted to investigate the effects of fat subtypes on GDM [48, 62]. It was found that saturated fats are sigificantly associated with the development of GDM, while polyunsaturated fats may be protective against GDM. On the other hand, information from observational studies suggests that a healthier diet, such as a Mediterranean diet, reduces the risk of GD [58, 63].

The MedDiet Project addresses the importance of the Mediterranean diet, highlights that eating fruitts, vegetables and whole grains may have preventive effects on GDM. A meta-analysis documented an important correlation between the risk of developing GDM and vitamin D deficiency [64]. A case-control study composed of 299 pregnant women diagnosed with GDM showed that adherence to the Mediterranean diet before pregnancy was associated with a lower risk of GDM [65]. Another study of 1076 pregnant women who followed a Mediterranean diet found a lower incidence of GDM and improved glucose tolerance [66].

Maternal Mediterranean diet and fetal/ neonatal insulin sensitivity

Insulin resistance impairs glucose metabolism, resulting in decreased glucose uptake in various tissues. It is well established that the intrauterine environment affects the growing offspring in a variety of metabolic ways, ranging from metabolic health to the development of metabolic diseases [67]. Intrauterine environment, glucose homeostasis and insulin homeostasis have been shownt to be affected by maternal diet. Pregnancy independent of maternal diet is characterized by increased development of insulin resistance, which may contribute to the development of GDM and some complex diseases in offspring later in life [68].

Importantly, animal studies have demonstrated changes in placental lipid transfer as a function of uterine lipid concentration and uterine circulation [69]. An increase in saturated fat in the womb has been shown to decrease insulin sensitivity and increase the glucose/insulin ratio in the child, resulting in inefficient glucose excretion. Insulin sensitivity has been found to increase with higher levels of omega-3 fatty acids. In addition, increased level of perinatal omega-6 fatty acids have been associated with the incidence of obesity in rodents [70]. Because the Mediterranean diet is high in monounsaturated fatty acids (MUFA), it has been shown to reduce the risk of cardiovascular disease by improving insulin sensitivity and blood lipids [71]. Another study highlights the importance of dietary habits in early pregnancy. Inadequate nutrition has a major impact on metabolic changes that cause prediabetic features at birth [72].

Maternal Mediterranean diet and neonatal lipoprotein profile and homocysteine

The studies mainly present findings on lipids and lipoproteins from infancy through adolescence and maturity. The presence of a proatherogenic environment, such as hypercholesterolemia during pregnancy, has previously been shown to increase oxidized lipids in the fetus and at birth. According to one study, lipid streaks grew relatively minimally during pregnancy, but their extent increased rapidly in later life compared to fetal development [73, 74].

Hyperhomocysteinemia is associated with the development of degenerative diseases such as kidney disease and neurological disorders. Therefore, in recent years, researchers have paid more attention to total homocysteine in serum [75]. For example, atherosclerosis is still a major cause of morbidity and mortality around the world [73]. There is evidence that the atherogenic process begins and is accelerated when levels of oxidised low-density lipoprotein (oxLDL) are elevated during pregnancy [2].

To date, the relationship between Mediterranean diet and many diseases has been studied. It has been suggested that inadeqauate consumption of Mediterranean diet is associated with lower risk of developing degenerative diseases However, the effects of the Mediterranean diet on coronary heart disease during pregnancy have not been adequately studied [73]. Mothers who follow a Mediterranean diet during pregnancy have been found to give birth to infants with low levels of insulinemia and insulin resistance [76]. Moreover, in recent years, research has focused on paraoxonase (PON-1) enzyme since it has antioxidant features and prevents low-density lipoproteins (LDL) from oxidation. Also, it has been suggested that this enzyme has pleiotropic antioxidant effects [77]. Furthermore, it has been observed that semisynthetic diets may contain compounds such as proteins, fiber, minerals, and vitamins that may affect lipids and lipoproteins. In one study, adherence to a Mediterranean diet during pregnancy was associated with lower homocysteine levels in Brazilian newborns [78]. In another study, following the Mediterranean diet was found to affect lipoprotein levels. A decrease in homocysteine levels was also observed, which was associated with improved glucose metabolism and higher maternal body weight [73].

Pregnancy and lipoprotein-associated coronary heart diseases

Undernutrition of fetuses in middle to late gestation results in disappropriate fetal growth, and leads to coronary heart disease [79, 80]. In particular, total fatty acids in plasma are significantly related to lipoprotein metabolism. In addition, several lipoprotein components such as cholesterol and saturated fat have been shown to be associated with cardiovascular health [81, 82].

Maternal hyperinsulinemia and increased tissue insulin sensitivity are some of the mechanisms leading to maternal fat deposition in the early stages of pregnancy [70, 73]. In later stages of pregnancy, low levels of lipoprotein lipase (LPL) and postheparin LPL activities are observed [70]. Changes in these metabolic processes reduce fat accumulation in maternal adipose tissue. Thus, increased lipolytic activity of adipose tissue leads to increased breakdown of fat deposits developed during the first trimester of pregnancy. In the liver, free fatty acids and glycerol are converted to acyl-CoA that leads to formation of glycerol-3-phosphate and triglycerides (TG), and packaged into very-low-density lipoprotein (VLDL). In addition, lipolysis increases and VLDL is produced and excreted in large amounts in later stages of pregnancy due to insulin resistance [70].

These metabolic processes in late pregnancy lead to an increase in VLDL levels and consequently, VLDL-TG and TG levels. In some pregnant women, transport of VLDL by cholesterol leads to an increase in total plasma cholesterol at the end of pregnancy. The increased level of VLDL in the late stages of pregnancy could therefore explain the increase in total cholesterol (TC) [70]. It is also suggested that the dietary mechanisms controlling low-density lipoproteins are less significant during pregnancy than in the pre-pregnancy period. Since TC seems to be the result of the temporary metabolic situation during pregnancy, TC should have a modest value in the diagnosis in pregnancy [73]. Detection of high levels of TC, could be used to determine neonatal risk for developing cardiovascular disease (CVD) [83]. In another study, CVD risk markers such as TC were shown to be detectable at 4 years of age at birth and in the respective parents [84].

The association between diet and lipoproteins in the fetus and at birth have not been extensively studied for several reasons. One of the possible reason was that the average levels of TC are similar in different populations of newborns [73]. According to the results of a study, Mediterranean diet during pregnancy may have an effect on systolic and diastolic blood pressure in children. In addition, the Mediterranean diet during pregnancy correlated with lower leptin levels, which may predict lower fat mass and TG in children [85].

Mediterranean diet and fertility

The influence of lifestyle factors on reproductive success has been extensively documented. To date, the influence of diet on fertility has been studied, focusing on individual foods and food categories [86]. In several studies, specific diet types and food groups have been widely studied, but the results have been incoclusive. According to some researchers, pregnancy rates after IVF have been increased by following a healthy diet [87]. Specifically, women who strictly adhered to the Mediterranean diet were found to have a lower risk of not becoming pregnant. According to the literature, male diet can have an impact on fertilization. Importantly, consumption of whole grains, cereals, vegetables, and fruits in large quantities is significantly associated with fertility and treatment outcomes [88]. According to some researchers, the high content of vitamin B6, folic acid and vegetable oils in the Mediterranean diet is one of the factors that can explain the positive effect of the Mediterranean diet on fertility [34]. Although the results of several studies are conclusive, further studies are needed to investigate the effects of the Mediterranean diet on IVF success rate [89].

Folate mechanism and congenital structural anomalies and fetal demise

The importance of the intrauterine environment for early embryonic development has been emphasized in recent years. In particular, folic acid has attracted the interest of researchers due to its importance in a number of clinical conditions [90]. Folate is necessary for cellular processes such as nucleotide synthesis and DNA repair. Furthermore, it acts as a cofactor for enzymes involved in one-carbon metabolism. Folate plays a central role in cell division and it is required during pregnancy and infancy. Folate plays a central role in cell division and is needed during pregnancy and infancy. During pregnancy, fetal, placental and maternal tissues need more folic acid [91, 92]. Folic acid deficiency, on the other hand, is associated with a number of diseases comprising birth defects and neural tube defects [93,94]. With an incidence of 0.2-10 per 1000 live births, neural tube defects (NTDs) are among the most common congenital anomalies of the central nervous system [95]. NTDs are serious birth defects caused by the failure of closure of the neural tube around 28th day after conception [96]. Genetic and environmental factors are involved in the pathogenesis of NTDs. Although the pathogenesis of NTDs is not yet clear, deficiencies in one-carbon metabolism are thought to be one of the causes the formation of NTDs [97].

Infants with anencephaly and spina bifida show several complications during their lifetime [98]. Randomized clinical trials have shown that folic acid consumption by mother during periconception is significantly associated with a reduced risk of developing NTDs [99, 100]. In addition, folic acid may also protect against other congenital abnormalities such as preeclampsia [101]. Folic acid intake and a folic acid-enriched diet are recommended by World Health Organization (WHO) and other government organizations in numerous countries for women of childbearing age. The incidence of NTDs was reduced by 50-75% with folic acid supplementation in the periconceptional period [102].

The synthetic version of the naturally occurring folates is folic acid (pteroylmonoglutamic acid) (pteroyl-L-poliglutamic acid). The basic difference between folic acid and folate is that the B9 vitamins differ in the amount of glutamate molecules they contain. Folates are found in many foods, primarily in green vegetables [103]. It has been shown that a maternal Mediterranean diet enriched with vitamin B12, niacin, iron and magnesium was significantly associated with spina bifida in the offspring [102]. In a study, western and prudent diets were compared. As a result, it has been shown that the that the children of women who followed the former dietary pattern were at higher risk for having cleft lip despite folic acid supplementation [102, 103]. Finally, a significant association was found between the risk of spina bifida (SB) and inadequate maternal consumption of a Mediterranean diet, possibly related to increased oxidative stress due to deficiencies of vitamins B6, B12, and folates [103].

Conclusion

In conclusion, pregnancy is a complicated process involving growth, development and maturation. Maternal nutrition's importance has undoubtedly been the subject of several studies, as it affects growth, maturation and fetal development. It has been shown that inadequate intake of essential macronutrients and micronutrients can negatively affect the outcome of pregnancy and neonatal health. Particularly, the periconceptional period is considered as a critical period for fetal development and health, as various malformations and pregnancy-related disorders occur during this time, including congenital anomalies, fetal losses, miscarriages, and preterm births. Importantly, a Mediterranean diet throughout pregnancy, especially in periconception, contributes to more appropriate growth from the first stage of pregnancy.

Acknowledgements

The authors would like to thank all the researchers who had conducted the studies.

Conflict of Interest

The authors have no conflict of interest to declare.

Author's Contributions

PT,HC conceptualized the content, and wrote the manuscript; MCE assisted with the revision of manuscript; PT

conceptualized the content and critically revised the manuscript. All authors read and approved the final manuscript.

References

[1] Spencer TE. Early pregnancy: Concepts, challenges, and potential solutions. Anim Front 2013;3:48-55. https://doi.org/10.2527/af.2013-0033

[2] Palinski W, Napoli C. The fetal origins of atherosclerosis: maternal hypercholesterolemia, and cholesterol-lowering or antioxidant treatment during pregnancy influence in utero programming and postnatal susceptibility to atherogenesis. FASEB J 2002;16:1348-60. https://doi.org/10.1096/fj.02-0226rev

[3] O'rahilly R, Müller F. Human growth during the embryonic period proper. In: Falkner F, Tanner JM. eds. Human Growth. Springer, Boston, MA 1986;1:245-6. https://doi.org/10.1007/978-1-4613-2101-9_13

[4] Odaka Y, Nakano M, Tanaka T, Kaburagi T, Yoshino H. The influence of a high-fat dietary environment in the fetal period on postnatal metabolic and immune function obesity. J Obes 2009;18:1688-94. https://doi.org/10.1038/oby.2009.513

[5] Ladipo OA. Nutrition in pregnancy: mineral and vitamin supplements. Am J Clin Nutr 2000;72:280-90. https://doi.org/10.1093/ajcn/72.1.280S

[6] Marangoni F, Cetin I, Verduci E, Canzone G, Giovannini M, Scollo P, Corsello G, Poli A. Maternal diet and nutrient requirements in pregnancy and breastfeeding. An Italian Consensus Document. Nutrients 2016;8:629. https://doi.org/10.3390/nu8100629

[7] Montagnoli C, Santoro CB, Buzzi T, Bortolus R. Maternal periconceptional nutrition matters. A scoping review of the current literature. J Matern Fetal Neonatal Med 2021;1-18. https://doi.org/10.1080/14767058.2021.1962843

[8] Cetin I, Berti C, Calabrese S. Role of micronutrients in the periconceptional period. Hum Reprod Update 2010;16:80-95. https://doi.org/10.1093/humupd/dmp025

[9] Mousa A, Naqash A, Lim S. Macronutrient and micronutrient intake during pregnancy: an overview of recent evidence. Nutrients 2019;11:443. https://doi.org/10.3390/nu11020443

[10] Rhind SM. Effects of maternal nutrition on fetal and neonatal reproductive development and function. Anim Reprod Sci 2004;83:169-81. https://doi.org/10.1016/j.anireprosci.2004.04.003

[11] Yee LM, Silver RM, Haas DM, Mercer BM, Iams J, Wing D, Parker B, Reddy UM, Wapner RJ, Grobman WA. Quality of periconceptional dietary intake and maternal and neonatal outcomes. Am J Obstet Gynecol 2020;223:121. https://doi.org/10.1016/j.ajog.2020.01.042

[12] De Giuseppe R, Bocchi M, Maffoni S, Del Bo E, Manzoni F, Cerbo RM, Porri D, Cena H. Mediterranean Diet and Lifestyle Habits during Pregnancy: Is There an Association with Small for Gestational Age Infants? An Italian Single Centre Experience. Nutrients 2021;13:1941. https://doi.org/10.3390/nu13061941

[13] Koletzko B, Godfrey KM, Poston L, Szajewska H, van Goudoever JB, de Waard M, Brands B, Grivell RM, Deussen, AR., Dodd JM, Patrogolab B, Zalewski BM. Nutrition during pregnancy, lactation and early childhood and its implications for maternal and long-term child health: the early nutrition project recommendations. Ann Nutr Metab 2019;74:93-106. https://doi.org/10.1159/000496471

[14] Danielewicz H, Myszczyszyn GDebinska A, Myszkal A, Boznanski A, Hirnle L. Diet in pregnancy — more than food. Eur J Pediatr 2017;176:1573-79. https://doi.org/10.1007/s00431-017-3026-5

[15] Flynn AC, Ho A, Pasupathy D. Nutrition in pregnancy. Obstet Gynaecol Reprod Med 2016;26:6-11. https://doi.org/10.1016/j.ogrm.2016.06.005

[16] Chen X, Zhao D, Mao X, Xia Y, Baker PN, Zhang H. Maternal dietary patterns and pregnancy outcome. Nutrients 2016;8:351. https://doi.org/10.3390/nu8060351

[17] Hofmeyr Gj, Lawrie TA Atallah ÁN,, DuleyL, Torloni MR. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database Syst Rev 2018;10:CD001059. https://doi.org/10.1002/14651858.CD001059.pub4

[18] Dawodu A, Akinbi H. Vitamin D nutrition in pregnancy: current opinion. Int J Womens Health 2013;5:333-43. https://doi.org/10.2147/IJWH.S34032

[19] Mariscal-arcas M, Rivas A, Monteagudo C, Granada A, Cerrillo I, Serrano FO. Proposal of a Mediterranean diet index for pregnant women. Br J Nutr 2009;102:744-49. https://doi.org/10.1017/S0007114509274769

[20] Gluckman PD, Hanson MA, Mitchell MD. Developmental origins of health and disease: reducing the burden of chronic disease in the next generation. Genome Med 2010;2:4. https://doi.org/10.1186/gm135

[21] Hales CN, Barker DJP. The thrifty phenotype hypothesis. Type 2 Diabetes. Br Med Bull 2001;60:5-20. https://doi.org/10.1093/bmb/60.1.5

[22] Bonatto F, Polydoro M, Andrades ME, Conte da Frota JML, Dal-pizzol F, Rotta LN, Souza DO, Perry ML, Moreira JCF. Effect of protein malnutrition on redox state of the hippocampus of rat. Brain Res J 2005;1042:17-22. https://doi.org/10.1016/j.brainres.2005.02.002

[23] Carmichael SL, Yang W, Feldkamp ML, Munger, RG, Siegariz AM, Botto LD, Shaw G. Reduced risks of neural tube defects and orofacial clefts with higher diet quality. Arch Pediatr Adolesc Med 2012;166:121-6. https://doi.org/10.1001/archpediatrics.2011.185

[24] Eskew AM, Wormer KC, Matthews ML, Norton HJ, Papadakis MA, Hurst BS. The association between fatty acid index and in vitro fertilization outcomes. J Assist Reprod Genet 2017;34:1627-32. https://doi.org/10.1007/s10815-017-1032-1

[25] Stephenson J, Heslehurst N, Hall J, Schoenaker DAJM, Hutchinson J, Cade JE, Poston L, Barrett G,, Crozier SR, Barker M, Kumaran K, Yajnik CS, Baird J, Mishra GD. Series Preconception health 1 Before the beginning: nutrition and lifestyle in the preconception period and its importance for future health. Lancet 2018;391:1830-41. https://doi.org/10.1016/S0140-6736(18)30311-8

[26] Steegers-theunissen PM, Twigt J, Pestinger V, Sinclair KD. The periconceptional period, reproduction and long-term health of offspring: the importance of one-carbon metabolism. Hum Reprod Update 2013;19:640-55. https://doi.org/10.1093/humupd/dmt041

[27] Barua S, Kuizon S, Junaid MA. Folic acid supplementation in pregnancy and implications in health and disease. J Biomed.Sci 2014;21:77. https://doi.org/10.1186/s12929-014-0077-z

[28] Bouwland-both MI, Steegers-theunissen RPM, Vujkovic M, Lesaffre EMEH, Mook-Kanomori DO, Hofman A, Lindemans J, Russcher H, Jaddoe VWV, Steegers EAP. A periconceptional energy-rich dietary pattern is associated with early fetal growth: the Generation R study. Int J Gynaecol Obstet 2012;120:435-45. https://doi.org/10.1111/1471-0528.12086

[29] Abdou RM, El Hawary GS, Saab AA. Effect of gestational Mediterranean diet intervention on newborn fat mass and cord blood leptin level. Gaz Egypt Paediatr Assoc 2020;63:30. https://doi.org/10.1186/s43054-020-00042-y

[30] Peraita-costa I, Gonzalez AL, Perales-Marin A, Sanz F, Llopis-Marales A, Morales-Suárez-Varela M. A retrospective cross-sectional population-based study on prenatal levels of adherence to the mediterranean diet: maternal profile and effects on the newborn. Int J Environ Res Public Health 2018;15:1530. https://doi.org/10.3390/ijerph15071530

[31] Fischer M, Stronati M, Lanari M. Mediterranean diet, folic acid, and neural tube defects. Ital J Pediatr 2017;43:74. https://doi.org/10.1186/s13052-017-0391-7

[32] Widmer RJ, Flammer,AJ, Lerman LO, Lerman A. The mediterranean diet, its components, and cardiovascular disease. Am J Med 2015;128:229-38. https://doi.org/10.1016/j.amjmed.2014.10.014

[33] Corsello G, Giuffrè M. Congenital malformations. Matern Fetal Neonatal 2012;25:25-9. https://doi.org/10.3109/14767058.2012.664943

[34] Karayiannis D, Kontogianni MD, Mendorou C, Mastrominas M, Yiannakouris N. Adherence to the Mediterranean diet and IVF success rate among non-obese women attempting fertility. Hum Reprod 2018;33:494-502. https://doi.org/10.1093/humrep/dey003

[35] Toledo E, Lopez-del Burgo C, Zambrana AR, Donazar M, Navarro-Blasco I, Martinez-Gonzalez AR, de Irala J. Dietary patterns and difficulty conceiving: a nested case – control study. Fertil Steril 2011;96:1149-53. https://doi.org/10.1016/j.fertnstert.2011.08.034

[36] Schoenaker DAJM, Soedamah-muthu SS, Callaway LK, Mishra GD. Prepregnancy dietary patterns and risk of developing hypertensive disorders of pregnancy: results from the Australian Longitudinal Study on Women's Health. Am J Clin Nutr 2015;102:94-101. https://doi.org/10.3945/ajcn.114.102475

[37] Assaf-balut C, De la Torre NG, Fuentes M, Duran A, Bordiu E, Del Valle L, Valerio J, Jimenez I, Herraiz MA, Izquierdo N, Torrejon MJ, De Miguel MP, Barabash A, Cuesta M, Rubio MA, Calle-Pascual AL. A high adherence to six food targets of the mediterranean diet in the late first trimester is associated with a reduction in the risk of materno-foetal outcomes: the st. Carlos Gestational Diabetes Mellitus Prevention. Nutrients 2019;11:66. https://doi.org/10.3390/nu11010066

[38] Tomkins A. Nutrition and maternal morbidity and mortality. Br. J Nutr 2001;85:93-99. https://doi.org/10.1049/BJN2000300

[39] Bao W, Bowers K, Tobias DK, Hu FB, Zhang C. Risk of gestational diabetes mellitus. Diabetes Care 2018;36:2001-8. https://doi.org/10.2337/dc12-2018

[40] Lamyian M, Hosseinpour-niazi S, Mirmiran P, Banaem LM, Goshtasebi A, Azizi F. Pre-pregnancy fast food consumption is associated with gestational diabetes mellitus among tehranian women. Nutrients 2017;9:216. https://doi.org/10.3390/nu9030216

[41] Henriksen T. Nutrition and pregnancy outcome. Nutr Rev 2006;64,19-23. https://doi.org/10.1301/nr.2006.may.s19-s23

[42] Pace ND, Desrosiers TA, Carmichael SL, Shaw GM, Olshan AF, Siega-riz AM. Antioxidant consumption is associated with decreased odds of congenital limb deficiencies. Paediatr Perinat Epidemiol 2017;32:90-9. https://doi.org/10.1111/ppe.12403

[43] Krapels IPC, Van Rooij IALM, Ocke MC, West CE, Van der Horst CMAM, Steegers-Theunissen, RPM. Maternal nutritional status and the risk for orofacial cleft offspring in Humans. J Nutr 2004;134:3106-13. https://doi.org/10.1093/jn/134.11.3106

[44] Sotres-alvarez D, Siega-riz AM, Herring AH, Carmichael SL, Feldkamp ML, Hobbs CA, Olshan AF, Defects B. Original contribution maternal dietary patterns are associated with risk of neural tube and congenital heart defects. Am J Epidemiol 2013;177:1279-88. https://doi.org/10.1093/aje/kws349

[45] Mohanty AF, Thompson L, Burbacher TM, Siscovick DS, Williams MA, Enquobahrie A. Periconceptional seafood intake and fetal growth. Pediatr Perinat Epidemiol 2015;329:376-87. https://doi.org/10.1111/ppe.12205

[46] Tuttolomondo A, Simonetta I, Daidone M, Mogavero A, Ortello A, Pinto A. Metabolic and vascular effect of the mediterranean diet. Int J Mol Sci 2019;20:4716. https://doi.org/10.3390/ijms20194716

[47] Martinez- Galiano JM, Olmedo-Requena R, Barrios- Rodriguez R, Amezcua-Prieto C, Bueno-Cavanillas A, Salcedo-Bellido I, Jimenez-Moleon JJ, Delgado-Rodriguez M. Effect of adherence to a mediterranean diet and olive oil intake during pregnancy on risk of small for gestational age infants. Nutrients 2018;10:1234. https://doi.org/10.3390/nu10091234

[48] Mahjoub F, Jemaa HB, Sabeh FB, Amor NB, Gamoudi A, Jamoussi H. Impact of nutrients and Mediterranean diet on the occurrence of gestational diabetes. Libyan J Med 2021;16:1. https://doi.org/10.1080/19932820.2021.1930346

[49] Gandevani SB, Amiri M, Yarandi RB, Tehrani FR. The impact of diagnostic criteria for gestational diabetes on its prevalence: a systematic review and meta - analysis. Diabetol Metab Syndr 2019;11. https://doi.org/10.1186/s13098-019-0406-1

[50] Saeedi M, Cao Y, Fadl H, Gustafson H, Simmons D. Increasing prevalence of gestational diabetes mellitus when implementing the IADPSG criteria: A systematic review and meta-analysis. Diabetes Res Clin Pract 2020;172:108642. https://doi.org/10.1016/j.diabres.2020.108642

[51] Mcintyre HD, Catalano P, Zhang C, Desoye G, Mathiesen ER, Damm P. Gestational diabetes mellitus. Nat Rev Dis Primers 2019;5. https://doi.org/10.1038/s41572-019-0098-8

[52] Li Y, Ren X, He L, Li J, Zhang S, Chen W. Maternal age and the risk of gestational diabetes mellitus: A systematic review and meta-analysis of over 120 million participants. Diabetes Res Clin Pract 2020;162:108044. https://doi.org/10.1016/j.diabres.2020.108044

[53] Fedullo AL, Schiattarella A, Morlando M, Raguzzini A, Toti E, De Franciscis P, Peluso I. Mediterranean diet for the prevention of gestational diabetes in the COVID-19 Era: Implications of Il-6 In Diabesity. Int J Mol Sci 2021;22:1213. https://doi.org/10.3390/ijms22031213

[54] Robitaille J, Grant AM. The genetics of gestational diabetes mellitus: evidence for relationship with type 2 diabetes mellitus Genet Med 2008;10:240-50. https://doi.org/10.1097/GIM.0b013e31816b8710

[55] Tobias DK, Zhang C, Chavarro J, Bowers K, Rich-edwards J, Rosner B, Mozaffarian D, Hu FB. Prepregnancy adherence to dietary patterns and lower risk of gestational diabetes mellitus. Am J Clin Nutr 2012;96:289-95. https://doi.org/10.3945/ajcn.111.028266

[56] Sotowski M, Mierzyński R, Czajkowska EP, Sotowski M, Szydełko-Gorzkowicz M. Nutrition as prevention factor of gestational diabetes mellitus: a narrative medicine. Nutrients 2021;13:3787. https//doi.org/10.3390/nu13113787

[57] Cao M, Zhang L, Chen T, Shi A, Xie K, Li Z, Chen Z, Wen J. Genetic susceptibility to gestational diabetes mellitus in a chinese population. Front Endocrinol 2020;11:247. https://doi.org/10.3389/fendo.2020.00247

[58] Donazar-ezcurra M, Burgo CL, Bes-rastrollo M. Primary prevention of gestational diabetes mellitus through nutritional factors: a systematic review. BMC Pregnancy and Childbirth 2017;17:30. https://doi.org/10.1186/s12884-016-1205-4

[59] Mijatovic-vukas J, Id LC, Cheng S, Stamatakis E, Louie J, Cheung NW, Markovic T, Ross G, Senior A, Brand-miller JC, Flood VM. Associations of diet and physical activity with risk for gestational diabetes mellitus: a systematic review and meta-analysis. Nutrients 2018;10:698. https://doi.org/10.3390/nu10060698

[60] Darling AM, Mitchell AA, Werler MM. Preconceptional iron intake and gestational diabetes mellitus. Int J Environ Res Public Health 2016;13:525. https://doi.org/10.3390/ijerph13060525.

[61] Zhang C, Liu S, Solomon CG, Hu FB. Dietary fiber intake, dietary glycemic load, and the risk for gestational diabetes mellitus. Diabetes Care 2006;29:2223-30 https://doi.org/10.2337/dc06-0266

[62] Bo S, Menato G, Lezo A, Signorile A, Bardelli C, De Michieli F, Massobrio M, Pagano G. Dietary fat and gestational hyperglycaemia. Diabetologia 2001;44:972-78. https://doi.org/10.1007/s001250100590

[63] Izadi V, Tehrani H, Haghighatdoost F, Dehghan A, Surkan PJ, Azadbakht L. Adherence to the DASH and mediterranean diets is associated with decreased risk for gestational diabetes mellitus. Nutrition 2016;32:1092-6. https://doi.org/10.1016/j.nut.2016.03.006

[64] Eckl MR, Brouwer-brolsma EM, Küpers LK. Maternal

adherence to the mediterranean diet during pregnancy: a review of commonly used a priori indexes. Nutrients 2021;13:582. https://doi.org/10.3390/nu13020582

[65] Requeana RO, Fernandez JG, Amezcua-Prieoto C, Moreno JM, Khan KS, Jimenez-Moleon JJ. Pre- pregnancy adherence to the mediterranean diet and gestational diabetes mellitus: a case-control study. Nutrition 2019;11:1003. https://doi.org/10.3390/nu11051003

[66] Karamanos B, Thanopoulou A, Anastasiou E, Assaad-Khalil S, Albache N, Bachaoui M, Slama CB, Ghomari H El, Jotic A, Lalic N, Lapolla A, Saab C, Marre M, Vassallo J, Savona-Ventura C. Relation of the Mediterranean diet with the incidence of gestational diabetes. Eur J Clin Nutr 2013;68:8-13. https://doi.org/10.1038/ejcn.2013.177

[67] Navarro E, Funtikova AN, Fitob M, Schröder H. PT Prenatal nutrition and the risk of adult obesity: Long-term effects of nutrition on epigenetic mechanisms regulating gene expression. J Nutr Biochem 2016;39:1-14. https://doi.org/10.1016/j.jnutbio.2016.03.012

[68] Oken E, Gillman MW. Fetal origins of obesity. Obes Res 2012;11:495-506. https://doi.org/10.1038/oby.2003.69

[69] Gesteiro Eva, Bastida S, Rodríguez B, Muniz FJS. Adherence to Mediterranean diet during pregnancy and serum lipid, lipoprotein and homocysteine concentrations at birth. Eur J Nutr 2014;54:1191-9. https://doi.org/10.1007/s00394-014-0798-5

[70] Herrera E, López-soldado I, Limones M, Amusquivar E, Ramos MP. Lipid metabolism during the perinatal phase, and its implications on postnatal development. Int J Vitam Nutr Res 2006;76:9831. https://doi.org/10.1024/0300-9831.76.4.216

[71] Bos MB, De Vries JHM, Feskens EJM, Van Dijk SJ, Hoelen D. WM, Siebelink E, Heijligenberg R, De Groot LCPGM. Effect of a high monounsaturated fatty acids diet and a Mediterranean diet on serum lipids and insulin sensitivity in adults with mild abdominal obesity. Nutr Metab Cardiovasc Dis 2010;20:591-8. https://doi.org/10.1016/j.numecd.2009.05.008

[72] Khan IY, Dekou V, Douglas G, Jensen R, Hanson MA, Poston L, Taylor PD, Taylor PDA. Fetal physiological programming a high-fat diet during rat pregnancy or suckling induces cardiovascular dysfunction in adult offspring. Am J Physiol Regul Integr Comp Physiol 2022;288:127-33. https://doi.org/10.1152/ajpregu.00354.2004.

[73] Gesteiro E, Sanchez-Muniz FJ, Rodilla ME, Bernal BE, Bastida S. Mediterranean diet and pregnancy. The Mediterranean Diet 2015:491-503. https://doi.org/10.1016/B978-0-12-407849-9.00044-0

[74] Celada P, Sánchez-Muniz FJ, Delgado-Pando G, Bastida S, Rodilla ME, Jiménez-Colmenero F, Olmedilla-Alonso B. Effects of improved fat meat products consumption on emergent cardiovascular disease 3 markers of male volunteers at cardiovascular risk. J Physiol Biochem 2016;72:669-78. https://doi.org/10.1007/s13105-016-0505-5

[75] Stover PJ. Polymorphisms in 1-carbon metabolism, epigenetics and folate-related pathologies. J Nutrigenet Nutrigenomics 2011;4:293-305. https://doi.org/10.1159/000334586

[76] Gesteiro E, Bernal BR, Bastida S, Muniz FJS. Maternal diets with low healthy eating index or mediterranean diet adherence scores are associated with high cord-blood insulin levels and insulin resistance markers at birth. Eur J Clin Nutr 2012;66:1008-15. https://doi.org/10.1038/ejcn.2012.92

[77] Aviram M, Rosenblat M, Bisgaier CL, Newton RS, Primo-Parmo SL, La Du BN. Paraoxonase inhibits high-density lipoprotein oxidation and preserves its functions. A possible peroxidative role for find the latest version: paraoxonase inhibits high-density lipoprotein oxidation and preserves. J Clin. Investig 1998;101:1581-90. https://doi.org/10.1172/JCI1649

[78] Couto FD, Moreira LMO, Santos DB, Reis MG, Gonçalves MS. Folate, vitamin B12 and total homocysteine levels in neonates from Brazil. Eur J Clin Nutr 2007;61:382-6. https://doi.org/10.1038/sj.ejcn.1602528

[79] Toth PP. Triglyceride-rich lipoproteins as a causal factor for cardiovascular disease. Vasc Health Risk Manag 2016;12:171-83. https://doi.org/10.2147/VHRM.S104369

[80] Shahid SU, Shabana NA, Rehman A, Humphries S. GWAS implicated risk variants in different genes contribute additively to increase the risk of coronary artery disease (CAD) in the Pakistani subjects. Lipids Health Dis 2018;17:89. https://doi.org/10.1186/s12944-018-0736-2

[81] Lewis GF, Rader DJ. New insights into the regulation of HDL metabolism and reverse cholesterol transport. Circ Res 2005;96:1221-32. https://doi.org/10.1161/01.RES.0000170946.56981.5c

[82] Lin C, Rajalahti T, Mjos SA, Kvalheim OM. Predictive associations between serum fatty acids and lipoproteins in healthy non-obese Norwegians: implications for cardiovascular health. Metabolomics 2016;12:6. https://doi.org/10.1007/s11306-015-0886-4

[83] Badiee Z, Kelishadi ÆR. Cord blood lipid profile in a population of iranian term newborns. Commun Biol 2007;29:574-9. https://doi.org/10.1007/s00246-007-9149-0

[84] Sattar N, Greer IANA, Galloway PJ, Packard CJ, Shepherd J, Kelly T, Mathers A, Biochemistry P. Lipid and lipoprotein concentrations in pregnancies complicated by intrauterine growth restriction. J Clin Endocrinol Metab 2015;84:128-30. https://doi.org/10.1210/jcem.84.1.5419

[85] Chatzi L, Rifas-Shiman SL, Georgiou V, Joung KE, Koinaki S, Chalkiadaki G, Margioris A, Sarri K, Vassillaki M, Vafeiadi M, Kogevinas M, Mantzoros C, Gillman MW, Oken E. Adherence to the Mediterranean diet during pregnancy and offspring adiposity and cardiometabolic traits in childhood. Pediatr obes 2017;12:47-56. https://doi.org/10.1111/ijpo.12191

[86] Gaskins AJ, Chavarro JE. Diet and fertility: a review. Am J Obstet Gynecol 2017;218:379-89 https://doi.org/10.1016/j.ajog.2017.08.010

[87] Sun H, Lin Y, Lin D, Zou C, Zou X, Fu L, Meng F, Qian W. Mediterranean diet improves embryo yield in IVF: a prospective cohort study. Reprod Biol Endocrinol 2019;17:73. https://doi.org/10.1186/s12958-019-0520-9

[88] Çekici H. Current nutritional factors affecting infertility and fertility. Ann Clin Lab Sci 2018;6. https://doi.org/10.21767/2386-5180.1000225

[89] Ricci E, Bravi F, Noli S, Somigliana E, Cipriani S, Castiglioni M, Chiaffarino F, Vignali M, Gallotti B, Parazzini F. Mediterranean diet and outcomes of assisted reproduction: an Italian cohort study. Am J Obstet Gynecol 2019;221:627 https://doi.org/10.1016/j.ajog.2019.07.011

[90] Gabory A, Attig L, Junien C. Developmental programming and epigenetics. Am J Clin Nutr 2011;94:1943-52. https://doi.org/10.3945/ajcn.110.000927

[91] Greenberg JA, Bell SJ, Guan Y, Yu HY. Folic acid supplementation and pregnancy: more than just neural tube defect prevention. Rev Obstet Gynecol 2011;4,52-9. https://doi.org/10.3909/riog0157

[92] Blom HJ, Shaw GM, Heijer M, Finnell RH. Neural tube defects and folate: case far from closed. Nat Rev Neurosci 2006;7:724-31. https://doi.org/10.1038/nrn1986

[93] Obican SG, Finnell RH, Mills JL, Shaw GM, Scialli AR. Folic acid in early pregnancy: a public health success story. FASEB J 2010;24:4167-74. https://doi.org/10.1096/fj.10-165084

[94] Copp AJ, Stanier P, Greene NDE. Neural tube defects: recent advances, unsolved questions, and controversies. Lancet Neurol 2013;12:799-810. https://doi.org/10.1016/S1474-4422(13)70110-8

[95] Botto LD, Moore CA, Khoury MJ, Erickson JD. Neural-tube defects. N Engl J Med 1999;341:1509-19. https://doi.org/10.1056/NEJM199911113412006

[96] Mirabelli M, Chiefari E, Arcidiacono B, Corigliano DM, Brunetti FS, Maggisano V, Russo D, Foti DP, Brunetti A.

Mediterranean diet nutrients to turn the tide against insulin resistance and related diseases. Nutrients 2020;12:1066 https://doi.org/10.3390/nu12041066

[97] Blencowe H, Kancherla V, Moorthie S, Darlison MW, Modell B. Estimates of global and regional prevalence of neural tube defects for 2015: a systematic analysis. Ann NY Acad Sci 2018;1414:31-46. https://doi.org/10.1111/nyas.13548

[98] Czeizel AE, Dobo M, Vargha P. Hungarian cohort-controlled trial of periconceptional multivitamin supplementation shows a reduction in certain congenital abnormalities. Birth Defects Res A Clin Mol Teratol 2004;70:853-61. https://doi.org/10.1002/bdra.20086

[99] De-Regil LM, Pena-Rosas JP, Fernandez- Gaxiola AC, Solon PC. Effects and safety of periconceptional oral folate supplementation for preventing birth defects. (Review). Cochrane Database Syst Rev 2015;14:12. https://doi.org/10.1002/14651858

[100] Bulloch RE, Lovell AL, Jordan VMB, Mccowan LME, Thompson JMD, Wall CR. Maternal folic acid supplementation for the prevention of preeclampsia: A systematic review and meta- analysis. Paediatr Perinat Epidemiol. 2018;32:346-57 https://doi.org/10.1111/ppe.12476

[101] Gomes S, Lopes C, Pinto E. Folate and folic acid in the periconceptional period: recommendations from official health organizations in thirty-six countries worldwide and WHO. Public Health Nutr 2016;19:176-89. https://doi.org/10.1017/S1368980015000555

[102] Taruscio D, Carbone P, Granata O, Baldi F, Mantovani A. Critical Review Folic acid and primary prevention of birth defects. Biofactors 2011;37:280-4. https://doi.org/10.1002/biof.175

[103] Pintó X, Vilaseca MA, Balcells S, Artuch R, Corbella E, Meco JF, Vila R, Pujol R, Grinberg D. A folate-rich diet is as effective as folic acid from supplements in decreasing plasma homocysteine concentrations. Int J Med Sci 2005;2:58-63. https://doi.org/10.7150/ijms.2.58

Correspondence: Pınar Tulay, Near East University, Faculty of Medicine, Department of Medical Genetics, 99138 Nicosia, Cyprus. E-mail: pinar.tulay@neu.edu.tr

How to cite this article: Çobanoğulları H, Ergoren MC, Dundar M, Bertelli M, Tulay P. Periconceptional Mediterranean diet during pregnancy on children's health. J Prev Med Hyg 2022;63(suppl.3):E65-E73. https://doi.org/10.15167/2421-4248/jpmh2022.63.2S3.9