

Review

The Impact of a Gluten-Free Diet on Pregnant Women with Celiac Disease: Do We Need a Guideline to Manage Their Health?

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Abstract: A healthy and balanced diet is a critical requirement for pregnant women as it directly influences both the mother's and infant's health. Poor maternal nutrition can lead to pregnancy-related complications with undesirable effects on the fetus. This requirement is equally important for pregnant women with celiac disease (CD) who are already on a gluten-free diet (GFD). Although the GFD is the sole treatment option for CD, it still presents some challenges and confusion for celiac women who wish to conceive. Poorly managed CD has been linked to miscarriages, preterm labor, low birth weight, and stillbirths. Current CD guidelines primarily focus on screening, diagnosis, treatment, and management but lack an evidence-based approach to determine appropriate energy requirements, recommended weight gain during pregnancy, target macronutrient distribution from the diet, the recommended intake of vitamins and minerals from diet and/or supplementation, timing for starting supplementation, and advised portions of gluten-free foods during pregnancy. We recommend and call for the development of such guidelines and/or authoritative papers in the future.

Keywords: gluten-free diet; celiac; pregnant; pregnancy; women; maternal; guideline; fetus; infant



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1. Introduction

Celiac disease (CD) is a multisystemic, chronic, immune-mediated inflammatory condition of the small intestine [1]. It occurs in genetically susceptible individuals upon ingestion of gluten, which is a storage protein found in wheat, rye, and barley [2]. The consumption of gluten in such individuals triggers a T-cell-mediated immune response that ultimately damages the enterocytes, leading to partial to total villous atrophy [3]. α -Gliadin, a component of gliadin, contains a 33-mer peptide that is particularly rich in proline–glutamine sequences. Intestinal and pancreatic enzymes are unable to digest these rigid amino acid sequences, resulting in their breakdown into relatively larger peptides. These larger peptides pass through intercellular junctions and enter the lamina propria, where they are deamidated by the tissue transglutaminase (tTG) enzyme. These deamidated gluten proteins are recognized by the HLA-DQ molecules, which activate CD4⁺ T lymphocytes and secrete interferon (IFN)- γ , leading to the destruction of the small intestinal mucosa [4]. CD has become a common intestinal disease, with a prevalence of more than 1% worldwide [5]. Classical symptoms of CD include diarrhea, weight loss, and abdominal pain. CD also includes extraintestinal manifestations, including iron-deficient anemia, headaches, fatigue, joint pain, and reduced bone mineral density [2,3]. CD is also associated with endocrine and neurological diseases, like type I diabetes, autism, and gluten ataxia [6]. The diagnosis of CD is made following the European Society for

Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) criteria, which suggest screening for CD based on symptoms and a first-line serological test, i.e., the IgA anti-tissue transglutaminase antibody (IgA, anti-tTG) test. They further recommend examination of characteristic changes in the duodenal biopsy (loss of villous structures, crypt hyperplasia, lymphoplasmacytic predominance, and increased density of intraepithelial lymphocytes) using duodenal endoscopy and biopsy, which is considered the gold-standard test for CD diagnosis [5].

Lifelong strict adherence to a gluten-free diet (GFD) is the only accepted treatment for CD so far [7]. To fulfill the requirements of the GFD, individuals with CD rely on commercially available gluten-free products (GFPs). GFPs with less than 20 mg/kg of gluten contamination are safe for daily consumption and can be labeled as gluten-free. This safe threshold (<20 mg/kg gluten) has been endorsed by the Codex Alimentarius and other agencies, such as the US Food and Drug Administration and the European Food Safety Authority (EFSA) [8].

Celiac disease is one of the common autoimmune conditions in females. Untreated CD in women is also associated with risks to fetal growth and their reproductive period [9–12]. The GFD requires extra care to meet the nutritional demands because the GFD/GFPs (naturally occurring or commercially available) provide less nutrition compared to their gluten-containing counterparts [13,14]. It has been reported that, among celiac patients who follow a long-term (over 2 years) GFD with good compliance, nutritional deficiencies still persist in 20–40% of patients [15]. Maternal CD may be a risk factor for key nutrients during pregnancy, such as folate, iron, calcium, vitamin D, and vitamin B₁₂ [16]. Females with CD planning to conceive need to ensure their nutrition is at its best before pregnancy to create a favorable environment for preimplantation and early differentiation for early fetal and placental development [17]. Additionally, during pregnancy, a GFD plan should be made to meet the energy and nutrient needs of both the mother and the infant to protect them from complications [18].

Available CD guidelines mainly focus on disease screening, diagnosis, treatment, and management but do not provide an evidence-based approach to determine the appropriate energy and nutrient requirements in pregnant women with CD. No international guideline or expert opinion providing recommendations regarding the energy, nutrient, supplement requirements, and gluten-free food portions for pregnant women with CD has been found. Therefore, in this review article, we aim to discuss the risk of a standard GFD (designed for patients with CD) on maternal celiac pregnancy and fetal development. We explored if there is a need for specific guidelines for pregnant women with CD already on a GFD or if there is a need for amendments to current CD guidelines to provide recommendations for a GFD with optimized nutrition to meet the nutrient needs of pregnant women with CD.

2. Celiac Disease, Pregnancy, and Fetal Development

An association between CD and pregnancy has long been recognized and different pregnancy-related difficulties have been reported [19]. In a systemic review, Saccone et al. reported that women with CD are at significantly higher risk of developing preterm birth, intrauterine growth restriction, stillbirth, low birth weight, and being small for gestational age [20]. The cause for reproductive abnormalities in CD has not been clearly understood. However, malnutrition and the autoimmune mechanism are considered two significant possibilities [21]. In the normal fertilization process, the female immune system usually induces tolerance towards the embryo, but this tolerance induction remains insufficient in a hyperactive immune system, such as in CD, which can reduce fertility and increase miscarriage risk [22]. Immune effects in untreated CD women may put placental function at risk by binding maternal autoantibodies to syncytiotrophoblast plasma membrane of the placenta [23]. Undigested gliadin peptides induce innate and adaptive T-cell-mediated immune responses [24]. The activated T cells secrete cytokines in T helper 1 and 2 patterns. The T helper 1 pattern induces crypt hyperplasia or villous atrophy, whereas T helper 2 pattern mostly results in the production of specific IgA auto-antibodies to tTG (EMA) in

patients with active CD [25]. The activation of T helper patterns may induce secondary autoimmunity and lead to extraintestinal disorders, such as autoimmune thyroiditis, type 1 diabetes, liver disease, and rheumatologic disorders, in patients with CD [26]. CD patients with extraintestinal disorders are at greater risk of developing adverse pregnancy outcomes [27]. It has also been noted that the miscarriage rate is about six times greater in untreated versus treated CD female patients [19]. Nevertheless, a long-term strict GFD can prevent recurrent miscarriages. According to a case–control study, the relative risk of abortion in maternal CD pregnancies already on a GFD decreases by nine times [28]. On the other hand, another study reported that approximately half of the study patients following a GFD conceived within 1–4 years [29]. Therefore, the nutritional needs of the GFD have become a promising hope in celiac women with infertility.

3. What Is a Gluten-Free Diet (GFD)

A GFD is a gluten-deprived diet specially developed for CD (and also recommended for other gluten-related disorders) and is currently the only accepted and effective treatment for CD [1]. It is based on the complete elimination of all gluten-containing foods from the diet, including gluten proteins found in wheat (gliadin), barley (hordeins), rye (secalins), and other closely related cereals [8]. A strict GFD gradually repairs the integrity of the small intestinal mucosa by restoring the histology of the small bowel villous and promoting small bowel healing. Adherence to a strict GFD improves celiac-related symptoms [30].

A GFD includes meat and its products, milk and its products, vegetables and fruits, and, from the grain group, rice, corn, and pseudocereals such as amaranth, quinoa, sorghum, and teff [31]. A description of gluten-free food is given in Figure 1.



Figure 1. Gluten-free foods. Naturally gluten-free grains (corn, rice, and pseudocereals such as amaranth, quinoa, sorghum, and teff); fruits (apple, pineapple, grape, melon, cherry, banana, pomegranate, etc.); vegetables (tomato, cucumber, parsley, mint, carrot, eggplant, lettuce, etc.); meat and their products (beef, chicken, fish, etc.); legumes (chickpea, bean, lentil, etc.); oil seeds (nut, walnut, almond, etc.), photos are from thenounproject.com (accessed on 21 January 2024).

Conversely, gluten-containing foods include wheat, barley, rye, oats, and products made from these grains such as starch, flour, bread, pasta, cake, etc. [31]. A description of gluten-containing food is given in Figure 2.

Adopting a GFD is difficult mainly due to its palatability, limited availability, and high cost [32]. However, poor adaptation to a GFD or an improperly balanced GFD (with an excess intake of fats and simple sugars) is often associated with complications such as an increased risk of malnutrition, nutrient deficiencies, obesity, cardiovascular risk, metabolic syndrome, and fatty liver [33]. It has been reported that metabolic syndrome can develop after 1 year of a GFD [34]. On the other hand, a GFD imposes a high treatment burden on

patients with CD in terms of purchasing and preparing foods, difficulty eating outside the home, concerns about the cost of food, and low taste acceptability [35].



Figure 2. Gluten-containing food. Food items containing high levels of gluten (wheat, rye, barley, semolina, spelt, kamut, etc.); food items without a gluten-free label (wheat starch, wheat bran, cracked wheat, and hydrolyzed wheat protein); food items that may contain gluten traces (emulsifiers, seasonings, edible food colors, chips, processed meat, French fries, sausages, canned food, soups, and tomato ketchup); gluten-removed drinks (brewed from gluten-containing grains), photos are from thenounproject.com (accessed on 21 January 2024).

4. The Importance of GFD Adherence Assessment in Celiac Pregnancy Follow-Up

To follow a GFD, patients with CD are referred to consult an experienced dietitian with prior experience in GFD diet counselling to receive a complete nutritional assessment and GFD guidance.

Nutritional Assessment in CD

Nutritional assessment is routinely performed as part of medical therapy, since nutritional status directly influences a patient's response to illness. Both nutrient deficiencies and excesses should be easily detectable with this evaluation. Van Megen et al. (2023) found that women with CD had an unbalanced diet with a higher intake of total and saturated fatty acids and a lower intake of fiber compared to the general population [36]. In another study, the anthropometric measurements (body cell mass index, fat-free mass index, appendicular skeletal muscle index, and phase angle) were found to be lower in patients with CD at diagnosis than in healthy controls. These findings emphasize the need and importance of nutritional assessment and follow-up for patients with CD [37].

Brief medical and dietary history (including feeding ability), anthropometric measures (e.g., weight and stature), and laboratory results are all part of a standard nutritional screening [38]. In-depth medical and dietary histories are part of a comprehensive nutritional evaluation, which includes a measure of dietary intake, a complete physical examination, further anthropometric evaluations (e.g., percentage weight loss, mid-arm muscle circumference, or body mass index (BMI)), body composition (using tools such as computed tomography and nuclear magnetic resonance, among others), hepatic biochemical markers (such as serum albumin level, transferrin, or retinol-binding protein), dynamometry, calorimetry, and the estimation of nutritional requirements [39]. In addition to these objective facts, a clinician's clinical judgment should be used to assess nutritional status. The final part of a nutritional evaluation is the estimation of dietary requirements [38].

Various governing bodies, including the Institute of Medicine (IOM), World Health Organization (WHO), and Food and Agriculture Organization (FAO), provide primary sources for information on requirements and recommendations of energy, nutrition, and dietary intake for healthy and pregnant women. However, there is no specific expert consensus for both patients with CD and maternal celiac pregnancy. This situation leads to variations in clinical practices and increases the risk of under- or over-estimation of energy and nutritional requirements. Failure to meet adequate energy and nutrient requirements during pregnancy negatively influences fetal growth and metabolic patterns, having adverse later-life metabolic effects for the offspring [40].

5. The Role of GFD in Reproductive Outcomes of Maternal Celiac Pregnancy

Adherence to a GFD has shown positive effects on reproductive outcomes [28,29,41]. However, some complications have also been reported in women on a GFD [42]. Undiagnosed CD or poor compliance with a GFD may lead to some nutritional deficiencies such as iron, vitamin B₁₂, folate, vitamin D, and calcium, which may further adversely impact outcomes both in the fertilization process and fetal development [31,43]. The effect of GFD on pregnancy outcomes is shown in Table 1.

Table 1. The effect of gluten-free diet on pregnancy outcomes.

Author	Year	Study Design	Number of Participants (F)	GFD Effect
Alecsandru et al. [41]	2019	Retrospective	690	GFD improved reproductive outcomes in women that followed a GFD
Ayoub et al. [42]	2017	Descriptive retrospective	173	The reproductive disorders associated with CD respond very well under GFD
Tursi et al. [29]	2008	Case–control	13	GFD adherence helps in conceiving (1–4 years with GFD adherence) in CD women with recurrent miscarriage
Ciacchi et al. [28]	1996	Case–control	94	GFD compliance shows incidence of abortion, low birth weight babies, and increased short breastfeeding periods in celiac women.

6. Nutritional Risk Factors in Maternal Celiac Pregnancy and the Influence on Fetus Development

Nutrient deficiency, often occurring in active CD, has historically been considered the main cause of gynecologic disorders and adverse pregnancy outcomes associated with the disease. Abnormal villous structure is considered a hallmark of CD, which generally results in malabsorption. It can be related to the insufficient intake of macro- and micro-nutrients in a GFD plan [31,44]. Since the major proximal parts of the intestine are affected in patients with CD, the most common nutrient deficiencies are iron, calcium folate, and vitamin B₁₂ absorbed from the ileum at the beginning of diagnosis. Additionally, calcium, phosphorus, and vitamin D deficiencies may develop due to the elimination of milk and dairy products from the diet due to the patient's malabsorption status or secondary lactose intolerance accompanying CD [31,44,45].

In addition, it has been reported that celiac women tend to have an unbalanced diet with a higher intake of total and saturated fatty acids and a lower intake of fiber compared to the general population [36]. Unbalanced dietary habits that result in a high BMI can be associated with pregnancy complications such as pre-eclampsia, gestational hypertension, and macrosomia [46]. In addition, during pregnancy, a GFD plan should be made to meet the energy and nutrient needs of both the mother and the infant to protect them from complications. Especially body mass index (BMI) in women is one of the influencing factors that affect pregnancy outcomes. In a study, the BMI of participants at diagnosis reported that 17.3% were underweight, 15.2% overweight, and 6.8% were obese [47]. The energy,

carbohydrates, and fiber intake of celiac women is found to be low in CD women [48]. According to a systematic review and meta-analysis results, the daily micronutrient intake of adult patients with celiac disease reported for iron 13.2 mg, calcium 1004.9 mg, and vitamin D 5.1 mcg [49].

Important nutrients (carbohydrates, folic acid, iron, Vitamin B₁₂ and D, etc.) associated with CD and the factors (weight gain and energy requirements) that influence fetal development are explained in the following section.

6.1. Energy Requirements

Energy requirements in pregnancy are defined as dietary requirements necessary to support optimal development of maternal tissues to support additional energy for fetal growth and development [50]. Energy demand increases due to the mother's weight gain and the development of maternal and fetal tissue. To meet this energy demand, the mother has to include extra energy in their diet plan, approximately 352–452 kcal in the first and third trimesters, respectively [51]. Many recommendations for energy and dietary intake are based on observational studies and expert consensus for healthy pregnant women [52]. A theoretical model was developed by Hytten and Chamberlain (1991) to estimate the energy requirements during pregnancy for well-nourished women [53]. However, the energy needs of well-nourished women in developed societies during pregnancy may vary compared to women of short stature or different weights in developing societies [52]. On the other hand, current energy formulations do not reflect the needs of pregnant women who are generally older, have more sedentary behaviors, have different body compositions, or are in specific groups such as CD.

It has been reported that the energy expenditure and substrate oxidation utilization change in individuals already following a GFD [54]. An important study that pays attention to increased energy expenditure and decreased energy capacity in celiac patients on a GFD is presented in [55]. These findings suggest that celiac-specific equations may be more correct for determining energy needs. Additionally, in maternal celiac pregnancy, different energy targets should be evaluated by accounting for all the factors that influence energy expenditure such as trimester, pre-pregnancy BMI, body composition, increasing energy demand, etc.

6.2. Body Mass Index (BMI)

A BMI is a ratio of weight-to-height. It has been developed to estimate the risk of being overweight or underweight in people [56]. Maternal pre-pregnancy BMI, gestational weight gain, and nutritional habits are associated with substantial risks for maternal and child health [57]. Generally, CD individuals have a lower BMI than the regional population at diagnosis [58]. Maternal BMI and weight gain or loss are related to the energy balance between food intake and energy expenditure. Based on the suggestions by the International of Medicine (IOM-2009), dietary energy intake can be determined by pre-pregnancy BMI and maternal body weight [18]. The maternal weight gain and energy recommendations for fetal development are given in Table 2.

As shown in Table 2, the IOM-2009 guideline categorizes gestational weight gain (GWG) based on pre-pregnancy BMI. According to this guideline, for women with a normal BMI (18.5–24.9 kg/m²), the recommended amount of weight gain during pregnancy is 11.5 kgs to 16.0 kgs and the recommended energy intake is 30 kcal/kg/day [59]. However, this guideline has not been updated since 2009 and there are no suggestions for groups with special diagnoses like CD. Maternal celiac pregnancy may need different weight gain and energy requirement targets according to their BMI classification for better outcomes of infant development. In addition, insufficient adherence to and/or an unbalanced GFD directly influences the BMI and nutritional status of patients, increasing the risk of pregnancy complications and affecting fetal development. Important factors that influence BMI are discussed below.

Table 2. The maternal weight gain and energy recommendation for fetal development according to pre-pregnancy BMI.

Healthy Women Pregnancy	Total Weight Gain **	Recommended Daily Energy Intake **	Maternal Celiac Pregnancy
Pre-pregnancy BMI (kg/m ²)	Range in kg	kcal/kg/day	
Underweight (<18.5)	12.5–18	36–40	N/A *
Normal weight (18.5–24.9)	11.5–16	30	N/A
Overweight (25.0–29.9)	7–11.5	24	N/A
Obese (≥30)	5–9	12–18	N/A

* No available data; ** based on (Mecacci, F., 2015 and IOM, 2009) [18,59].

6.3. Carbohydrates

Carbohydrates are the primary source of fuel for the human body and, most significantly, the brain is comprised of carbohydrates. Because glucose generated from carbohydrates is the primary fuel utilized for intrauterine growth, pregnant women require the energy provided by carbohydrate consumption to grow a healthy baby [60,61]. While the main carbohydrate and energy source of the global dietary pattern is wheat and its derivatives, the main grain sources of the GFD are maize and rice, minor cereals (sorghum, teff, millet, and wild rice), and pseudo-cereals (quinoa, chia, and amaranth) [31,62,63]. Studies have found that CD individuals have a low carbohydrate intake for several reasons, such as the tastelessness of alternative grain sources, limited availability, and the high cost of gluten-free alternatives [64–66]. The daily recommended intake (DRI) for carbohydrates during pregnancy is at least 175 g/d for normal women but there is no specific suggestion about the carbohydrate requirements of celiac pregnant women [67]. A GFD is characterized by its low complex carbohydrate and fiber intakes [64]. It is known that low carbohydrate intake has negative effects on fetal growth and development by leading to energy deficiency [60]. For this reason, the optimal complex carbohydrate and fiber intakes in maternal celiac pregnancy should be determined based on future updated guideline suggestions that will consider the disadvantages of GFD.

6.4. Folic Acid

Folic acid is an essential vitamin for the development of the brain and spinal cord and must be supplemented for at least 1–3 months before conception to prevent neural tube defects [65]. In normal conditions, the neural tube is developed by day 28 of gestation.

In folic acid deficiency, an opening at the lower end of the spine can produce spina bifida that does not close fully, and this defect can lead to anencephaly, which is the complete inability of the brain to develop [66]. Pregnancy complications that are related to folic acid deficiency primarily include neural tube defects, and folic acid supplementation has a 72% protective effect [65].

Folic acid is also involved in the structure of enzymes involved in the production of red blood cells and hemoglobin. In folic acid deficiency, the number of white and red blood cells decreases, which can lead to megaloblastic anemia [68].

The main sources of folic acid in the diet are organ meats, legumes, and green leafy vegetables [69]. Although these food groups are even not forbidden on a GFD, folic acid deficiency is highly reported in patients with CD, even in those who adhere to a GFD [31,70]. According to the DRI, the recommended folic acid requirement for pregnant women is approximately 600 mcg/day, but there are no studies on the folic acid requirements for pregnant women with CD [71,72]. The requirement of folic acid in maternal CD may be increased due to intestinal malabsorption. Therefore, specific suggestions for folic acid intake in maternal CD can be developed for better pregnancy outcomes by high-quality research studies.

6.5. Iron

Iron reserves in the mother at the time of conception are an excellent indicator of maternal iron status as well as the likelihood of iron deficiency and anemia later in pregnancy [58]. Because iron plays an important role in the production of hemoglobin, cellular oxygen delivery, electron transport, and enzymatic activity, the iron requirements of pregnant women are significantly increased [72]. This is because the increased oxygen demand, which rises dramatically by 20 to 30%, the growth of the fetus, and the development of appendages, including the placenta, all contribute to an increased need for iron [73]. Iron deficiency anemia (IDA) is the most recognized type of anemia in patients with CD and may be present in over half of patients at the time of diagnosis [74]. Maternal anemia may increase the risk of low birth weight or premature babies. Therefore, dietary and supplemental iron support is important for healthy infant development [73]. Diets contain relatively small quantities of heme iron derived from meat and fish, which is always well absorbed, so the iron bioavailability of foods of animal origin is higher than that of foods of plant origin [74]. Even though a GFD contains animal foods, iron deficiency anemia is commonly reported in individuals with CD [31,75].

According to expert opinions, pregnant women's elemental iron requirements are between 16 and 27 mg, but there is no specific recommendation for maternal celiac pregnancy [72,76]. Therefore, the amount of dietary iron sources and the dosage of iron supplementation need to be determined carefully when planning the diet of pregnant women with CD.

6.6. Calcium

Fetal growth requires a high demand of maternal calcium, especially in the third trimester [77]. Maternal calcium intake is essential, and this high demand is to meet increased intestinal calcium absorption. Intestinal malabsorption of calcium may lead to intrauterine growth restriction, low birth weight, poor bone mineralization, and preterm birth, whereas maternal risks include hypertension and pre-eclampsia [78]. The dietary calcium intake is mainly from dairy products, but the calcium intake is reported to be low in patients with CD because of intestinal malabsorption or lactose intolerance [31,45]. Calcium intakes of 1000 mg/day are recommended for pregnant women by the EFSA and FAO of the United Nations, whereas calcium intakes of 950–1000 mg/day are recommended for non-pregnant adults (aged 19–50). There is no specific recommendation for CD [72,79,80]. More than 50% of untreated patients with CD have bone loss detected by bone densitometry (dual-energy X-ray absorptiometry: DEXA) [81]. According to one of the systematic reviews, GFD adherence resulted in partial recovery of bone density in one year, and full recovery in five years [82]. Undiagnosed celiac patients, or those between 1 and 5 years after diagnosis, remain at great risk in terms of calcium requirements that influence fetal development. Calcium intake requirements may differ in pregnant women with CD, which depends on the diagnosis period and GFD adherence.

6.7. Vitamin D

During pregnancy, women need to maintain enough vitamin D levels, especially to meet their unborn children's calcium needs for bone mineral growth [83]. Reduced bone mineral density is frequently found in adults with CD, and dietary guidelines recommend vitamin D supplementation for both adults and children with CD [84]. Vitamin D supplementation reduces the risk of gestational diabetes, pre-eclampsia, and possibly the risk of low birth weight and being small for gestational age [85]. The recommended intake of vitamin D set by expert opinion is 600 IU/d but, in terms of maternal CD, there is currently insufficient evidence to support definite clinical recommendations regarding vitamin D supplementation during pregnancy [72,86].

6.8. Vitamin B₁₂

Vitamin B₁₂ plays an active role in the formation and myelination of nerve cells. In addition, it is essential for DNA synthesis, cellular energy production, and the enzyme system that helps regulate homocysteine levels [87]. In cases of vitamin B₁₂ deficiency, homocysteine levels increase in the blood, which is associated with pre-eclampsia, a common condition in pregnancy. Therefore, it is recommended to maintain a blood vitamin B₁₂ level of 300 ng/L before conception since a level of vitamin B₁₂ < 250 ng/L during pregnancy increases the risk of neural tube defects [88]. The requirement of vitamin B₁₂ in pregnant women differs from 2.6 to 4.5 mcg/day. The recent research has not determined vitamin B₁₂ requirements of a pregnant women with CD. Dietary sources of vitamin B₁₂ are animal origin, especially red meat, because of higher bioavailability than plant-based sources [87]. Although animal meats are not prohibited on the GFD, vitamin B₁₂ deficiency can still occur in people with CD, even with supplementation usage [89,90]. Therefore, it is important to regularly check vitamin B₁₂ levels in the blood, especially in pregnant women with CD, for the fetus and infant development.

The GFD becomes a nutritional connection between the fetus and pregnant woman with CD. Therefore, a GFD should be properly planned to meet the nutritional demands of the fetus. However; the key nutritional risk factors in maternal celiac pregnancy that still need to be addressed are summarized in Figure 3.

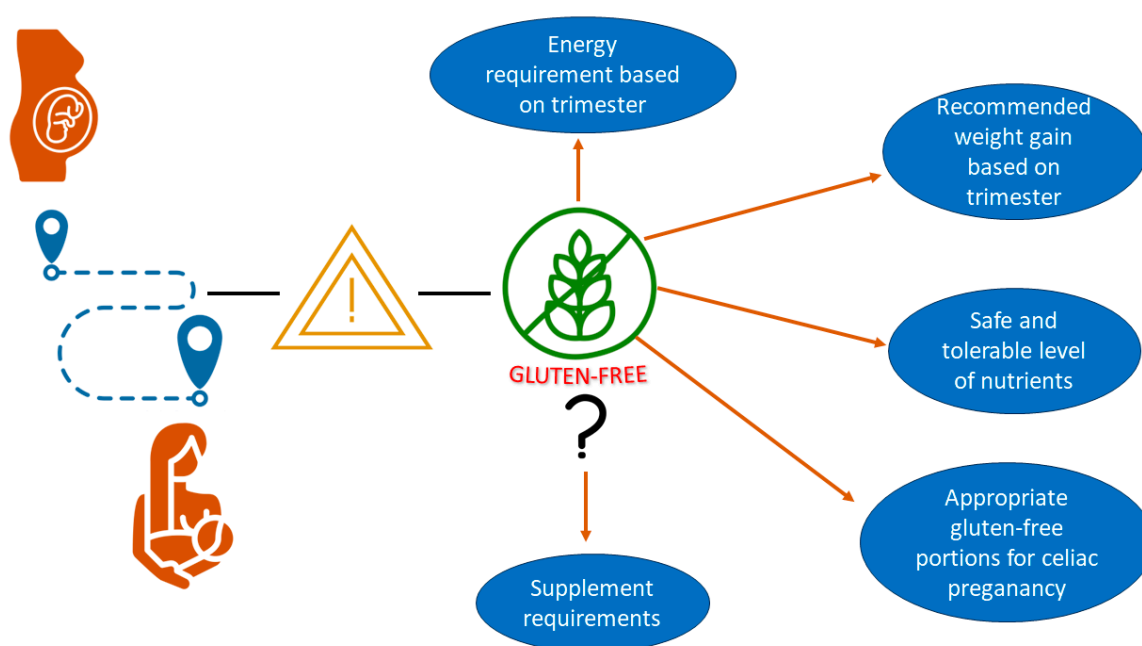


Figure 3. Main nutritional risk considerations in maternal celiac pregnancy (icons are from thenounproject.com, accessed on 21 January 2024).

7. Current Status of Nutritional Guidelines for Pregnant Women with Celiac Disease

Nutrition during pregnancy is a primary factor affecting fetal development, but available CD guidelines do not provide an evidence-based approach to determine the appropriate energy and nutrient requirements for pregnant women with CD. These guidelines also lack information on the most effective and safe dosages, the optimal dosing regimen (daily, intermittent, or single doses), the timing and initiation of vitamin–mineral supplementation, and the interactions of vitamin and minerals.

Reduced levels of iron, folate, vitamin B₁₂, vitamin D, and calcium are common in untreated CD, and some of these deficiencies can persist even after the removal of gluten from the diet or during a short window of supplementation [70]. The recommended intake of these nutrients for normal pregnant women is summarized in Table 3, but there is no

available information regarding maternal celiac pregnancy. The celiac patients routinely use vitamin–mineral supplementation in varying doses (Table 3). Considering the vital effects of these vitamins and energy requirements on fetal development, GFD must be individualized in terms of individual dietary risks for each pregnant celiac woman. The recommendations of supplementation for these groups are generally based on blood level of micronutrients and personalized recommendations. On the other hand, there is no categorization in terms of adequate intake or tolerable upper-limit definitions of nutrients [15]. It seems that celiac patients tend to use higher doses of vitamin–mineral supplements in clinical practice than the recommended intake of healthy individuals (Table 3).

Table 3. Summary of tolerable upper limits and recommendations for intake of nutrients in healthy, pregnant, and celiac women groups.

		Safety Limit (Tolerable Upper Limit) per Day				Recommended Intake Level from Food or Supplements per Day			
	Food Sources	Normal Women	Pregnant Women	Celiac Patients	Celiac Pregnant Women	Normal Women	Pregnant Women	Celiac Patients	Celiac Pregnant Women
Folic acid	Legumes, leafy green vegetables, broccoli, asparagus, and avocado	EU and US: 1000 mcg	EU and US: 1000 mcg	N/A	N/A	EU: 330 mcg US: 400 mcg	EU and US: 400–600 mcg	a. 800 mcg/day b. 1 mg/day of folic acid for 3 months and once diarrhea improves 400–800 mcg/day	N/A
Iron	Red meat; plant source such as legumes, nuts, and dark green vegetables is poorly absorbed	EU: No adequate data to derive a tolerable upper limit. US: 45 mg	None set in the EU; although supplementation in the absence of deficiency is not recommended US: 45 mg based on gastrointestinal side effects only	N/A	N/A	EU: 16 mg US: 18 mg	EU: 16 mg US: 27 mg	Iron supplements (325 mg) 1–3 tablets based on initial ferritin level until iron stores are restored. Consider i.v. iron for severe symptomatic iron deficiency anemia or intolerance of oral iron	N/A
Vitamin B ₁₂	Animal products such as meat, eggs, dairy, and fish	None set	None set; usual intakes 35 mcg, but 1000 mcg in malabsorption is commonly administered	N/A	N/A	EU: 4 mcg US: 2.4 mcg	EU: 4.5 mcg US: 2.6 mcg	a. 500 mcg/day b. 1000 mcg orally until the level is normal and then consider daily gluten-free multivitamin/mineral supplement	N/A
Vitamin D	Sun exposure	EU and US: 4000 IU	EU: and US: 4000 IU	N/A	N/A	EU and USA: 600 IU	EU: and US: 600 IU although this is highly conservative and 1500 IU may be better to reach optimal levels.	Vitamin D: 1000 (or more-based serum level) U.I./day or 50,000 IU. weekly if level is <20 ng/mL.	N/A
Calcium	Dairy, nuts, tofu, and tinned fish with bones	EU: 2500 mg US: 2000 mg	EU: and US: 2500 mg	N/A	N/A	EU: 950–1000 mg US: 1000 mg	US: and EU: 1000 mg	Calcium recommended intake of calcium, including supplementation, for patients with CD is 1200–1500 mg/day.	N/A

Adapted from [15,91], N/A: no available data, EU: European Union, US: United States, IU: International Unit.

While a clear explanation has been provided for normal pregnancy, significant limitations exist in evaluating the exact limit of evidence needed to make dietary recommendations, and it is still a big challenge to determine the correct levels of energy and nutritional requirements for more specific groups, such as maternal celiac pregnancy. The nutritional research challenges often include large individual differences in maternal adaptation to pregnancy, difficulties in accurately measuring maternal diet, ethical and practical issues of experimenting with pregnant people, challenges in determining the effects of specific nutrients in the context of the entire diet, and the lack of a good animal model that can be directly extrapolated to humans [92].

In addition, the randomized nutritional control methodology in pregnancy has some different steps from drug/supplement utilization because it may be an ethical issue to reduce directly nutrient intakes in pregnant women for comparison as a “control” group. The control group may be selected according to malnutrition situation and/or who has a lower BMI or different body composition.

Even though the usage of supplementations in pregnancy is common, there is not a local and/or global authority to approve dietary supplements for safety and effectiveness or to approve their labeling for clinical usage yet [91,93,94]. If the dietary intake of energy, macro-, and micronutrients is sufficient from the diet and the nutrition indicators in blood are in the normal range, the recommended intake and/or tolerable upper limits of supplementation usage need to be proven by randomized control trials for each trimester between healthy and celiac pregnancy (Table 3).

Nutrient deficiencies in CD may also develop over time, which are not always resolved during a short or long window of supplementation. Especially in celiac patients who have followed a GFD with supplementation usage for more than 2 years with good compliance, it has been reported that nutritional deficiencies still persist in 20–40% of patients [15]. It could be argued that this is even more important during pregnancy, as beginning supplements in the first or second trimester may not be a sufficient time frame in which to affect the development of the fetus [91]. On the other hand, the energy and dietary requirement in celiac pregnancy needs to be categorized by each trimester to prevent fetal complications [95].

Therefore, we need specific guidelines and/or position papers to determine the nutritional needs of pregnant women or other specific groups. Nutritional guidelines and/or position papers are the primary reference sources to determine nutrition and dietetic management in clinical practice. Authorities around the world that regularly publish nutritional guidelines include the American Society for Parenteral and Enteral Nutrition (ASPEN) [96], the European Society for Clinical Nutrition and Metabolism (ESPEN) [97], ESPGHAN [98], the North American Society For Pediatric Gastroenterology, Hepatology & Nutrition (NASPGHAN) [99], the Food and Agriculture Organization (FAO) [93], and the World Health Organization (WHO) [100].

These authorities frequently published dietary guidelines between 2015 and 2020 about allergies, critical illness, neonatal nutrition, pediatric nutrition, parenteral and enteral nutrition, micronutrients, probiotics, and malnutrition [96–102]. The current elaboration on the nutrition and dietetic management of illnesses includes some critical points. For example, ESPGHAN is recommended for children with neurological impairment, Schofield, and the Andrew et al. equations to estimate their calorie needs [103]. On the other hand, mid-upper arm circumference and triceps skin folds are suggested for use to evaluate the nutritional status of children with end-stage liver disease [104].

However, to plan the nutritional needs of patients with CD, guidelines from Europe and America and various scientific authorities are used. These guidelines generally aim to identify effective strategies for the diagnosis and follow-up of CD [105]. However, the ESPGHAN guideline is widely accepted and provides directions for CD screening, diagnosis, treatment, and management [106]. The most recent position paper published by ESPGHAN (2022) is related to the management and follow-up of children and adolescents with CD. This guideline primarily focuses on 10 questions: (1) Is the clinical nutrition and dietetic follow-up and management of CD needed? (2) Who should do the follow-up of which patients, and what is the role of the dietitian? What is the role of self-care and e-health? (3) What should be the frequency of follow-up, and what should be assessed? (4) Questions related to adherence to a GFD, such as the role of detecting gluten immunogenic peptides (GIPs) or new nutritional indicators in the assessing compliance to a GFD. (5) Questions related to common issues during follow-up and management, such as how to treat anemia and/or sarcopenia or how chronic tiredness can be controlled in CD. (6) Questions about specific issues during follow-up and management (i.e., how to approach persistent high serum levels of antibodies against tissue-transglutaminase). (7) Should the quality of life (QOL) be assessed during follow-up and, if so, how? (8) Should the follow-up of children

with special situations be different from that of the average CD patient? (9) How to improve communication: to parents? To patients? (10) How to organize the transition from pediatric care to adult health care [107]. However, there are no nutritional guidelines that explain nutritional demands of most common comorbid situations in CD such as type 1 diabetes, pregnancy, thyroiditis, etc. Guidelines developed for the diagnosis and follow-up of patients with CD are inadequate for experts to determine the energy and nutrient needs for special situations such as pregnancy. As the age of celiac diagnosis increases, especially in the female age group, gluten-free nutrition guidelines need to be more detailed.

8. Expectations from Guidelines for Pregnant Women with Celiac Disease

The main expectations of nutritional and dietetic guidelines in pregnancy with CD should be to provide advice on what to eat and drink to meet nutrient needs, promote health, and prevent disease. Alternatively, disease-based clinical guidelines are systematically developed, evidence-based/evidence-informed statements and recommendations that assist and guide practitioner and patient decisions about appropriate nutrition care for specific clinical circumstances. This includes but is not limited to the role of specific diagnostic and treatment modalities in managing patients. Clinical guidelines are developed by multidisciplinary panels of experts based on evidence from a rigorous systematic review and evaluation of the published medical and health literature. Limited clinical nutritional trials in celiac patients prevent the development of high-level recommendations, and variations between expert opinions may lead to over- or underestimation of nutritional needs, which directly influences fetal development.

9. What Problems Should Guidelines for Pregnant Women with Celiac Disease Solve?

According to our nutrition and clinical dietetic experiments, the most common concerns for maternal celiac pregnancies include, but are not limited to, determining the most appropriate energy formulations and requirements, the recommended weight gain during pregnancy, the target macronutrient distribution from the diet, the recommended intake of vitamin and minerals from diet and/or supplementation, the timing and dosage of supplementation, and the advised gluten-free food portions during pregnancy and new nutritional and clinical indicators to follow up diet adaptation.

10. Conclusions

Available guidelines for CD mainly focus on screening, diagnosis, treatment, and management but do not provide an evidence-based approach to determine the appropriate energy and nutrient requirements for pregnant women with CD. There is a need for specific guidelines or amendments to the current CD guidelines to provide recommendations on a GFD with optimized nutrition to meet the nutrient needs of pregnant women with CD for pregnant women. Such guidelines should suggest the appropriate amount of energy requirements and formulations, recommended weight gain during pregnancy, target macronutrient distribution from the diet, the recommended intake of vitamins and minerals from diet and/or supplementation, the starting timing, duration and dosage of supplementation, and the advised gluten-free food portions during pregnancy and new nutritional and clinical indicator to follow up diet adaptation. We recommend and advocate for developing such guidelines and/or authoritative papers in the near future.

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References

1. Danowski, L.; Brand, L.G.; Connolly, J. Gluten-free diets, coeliac disease and associated disorders. *Fam. Pract.* **2003**, *20*, 607–611. [[CrossRef](#)] [[PubMed](#)]
2. Catassi, C.; Fasano, A. Clinical practice: Celiac disease. *N. Engl. J. Med.* **2012**, *367*, 2419–2426.
3. Green, P.H.; Cellier, C. Celiac disease. *N. Engl. J. Med.* **2007**, *357*, 1731–1743. [[CrossRef](#)] [[PubMed](#)]
4. Bilodeau, D.; Crémieux, P.-Y.; Jaumard, B.; Ouellette, P.; Vovor, T. Measuring hospital performance in the presence of quasi-fixed inputs: An analysis of Québec hospitals. *J. Prod. Anal.* **2004**, *21*, 183–199. [[CrossRef](#)]
5. Ashton, J.J.; Smith, R.; Smith, T.; Beattie, R.M. Investigating coeliac disease in adults. *BMJ* **2020**, *369*, m2176. [[CrossRef](#)] [[PubMed](#)]
6. Fasano, A. Systemic autoimmune disorders in celiac disease. *Curr. Opin. Gastroenterol.* **2006**, *22*, 674–679. [[CrossRef](#)] [[PubMed](#)]
7. Ciacci, C.; Ciclitira, P.; Hadjivassiliou, M.; Kaukinen, K.; Ludvigsson, J.F.; McGough, N.; Sanders, D.S.; Woodward, J.; Leonard, J.N.; Swift, G.L. The gluten-free diet and its current application in coeliac disease and dermatitis herpetiformis. *United Eur. Gastroenterol. J.* **2014**, *3*, 121–135. [[CrossRef](#)] [[PubMed](#)]
8. Aljada, B.; Zohni, A.; El-Matary, W. The gluten-free diet for celiac disease and beyond. *Nutrients* **2021**, *13*, 3993. [[CrossRef](#)] [[PubMed](#)]
9. Morris, J.; Adjukiewicz, A.; Read, A. Coeliac infertility: An indication for dietary gluten restriction? *Lancet* **1970**, *295*, 213–214. [[CrossRef](#)]
10. Ferguson, R.; Holmes, G.; Cooke, W. Coeliac disease, fertility, and pregnancy. *Scand. J. Gastroenterol.* **1982**, *17*, 65–68. [[CrossRef](#)]
11. Sher, K.S.; Mayberry, J.F. Female fertility, obstetric and gynaecological history in coeliac disease. *Digestion* **1994**, *55*, 243–246. [[CrossRef](#)] [[PubMed](#)]
12. Smecuol, E.; Mauriño, E.; Vazquez, H.; Pedreira, S.; Niveloni, S.; Mazure, R.; Boerr, L.; Bai, J.C. Gynaecological and obstetric disorders in coeliac disease: Frequent clinical onset during pregnancy or the puerperium. *Eur. J. Gastroenterol. Hepatol.* **1996**, *8*, 63–68. [[CrossRef](#)] [[PubMed](#)]
13. Jamieson, J.A.; Weir, M.; Gougeon, L. Canadian packaged gluten-free foods are less nutritious than their regular gluten-containing counterparts. *PeerJ* **2018**, *6*, e5875. [[CrossRef](#)]
14. Taetzsch, A.; Das, S.K.; Brown, C.; Krauss, A.; Silver, R.E.; Roberts, S.B. Are gluten-free diets more nutritious? An evaluation of self-selected and recommended gluten-free and gluten-containing dietary patterns. *Nutrients* **2018**, *10*, 1881. [[CrossRef](#)] [[PubMed](#)]
15. Rondanelli, M.; Faliva, M.A.; Gasparri, C.; Peroni, G.; Naso, M.; Picciotto, G.; Riva, A.; Nichetti, M.; Infantino, V.; Alalwan, T.A.; et al. Micronutrients dietary supplementation advices for celiac patients on long-term gluten-free diet with good compliance: A review. *Medicina* **2019**, *55*, 337. [[CrossRef](#)] [[PubMed](#)]
16. Stazi, A.V.; Mantovani, A. A risk factor for female fertility and pregnancy: Celiac disease. *Gynecol. Endocrinol.* **2000**, *14*, 454–463. [[CrossRef](#)] [[PubMed](#)]
17. Kaiser, L.L.; Allen, L. Position of The American dietetic association: Nutrition and lifestyle for a healthy pregnancy outcome. *J. Am. Diet. Assoc.* **2002**, *102*, 1479–1490. [[CrossRef](#)] [[PubMed](#)]
18. Mecacci, F.; Biagioni, S.; Ottanelli, S.; Mello, G. Nutrition in pregnancy and lactation: How a healthy infant is born. *J. Pediatr. Neonatal Individ. Med. (JPNIM)* **2015**, *4*, e040236.
19. Ogborn, A. Pregnancy in patients with coeliac disease. *BJOG Int. J. Obstet. Gynaecol.* **1975**, *82*, 293–296. [[CrossRef](#)]
20. Saccone, G.; Berghella, V.; Sarno, L.; Maruotti, G.M.; Cetin, I.; Greco, L.; Khashan, A.S.; McCarthy, F.; Martinelli, D.; Fortunato, F.; et al. Celiac disease and obstetric complications: A systematic review and metaanalysis. *Am. J. Obstet. Gynecol.* **2016**, *214*, 225–234. [[CrossRef](#)]
21. Tersigni, C.; Castellani, R.; de Waure, C.; Fattorossi, A.; De Spirito, M.; Gasbarrini, A.; Scambia, G.; Di Simone, N. Celiac disease and reproductive disorders: Meta-analysis of epidemiologic associations and potential pathogenic mechanisms. *Hum. Reprod. Updat.* **2014**, *20*, 582–593. [[CrossRef](#)]
22. Sen, A.; Kushnir, V.A.; Barad, D.H.; Gleicher, N. Endocrine autoimmune diseases and female infertility. *Nat. Rev. Endocrinol.* **2014**, *10*, 37–50. [[CrossRef](#)] [[PubMed](#)]
23. Anjum, N.; Baker, P.N.; Robinson, N.J.; Aplin, J.D. Maternal celiac disease autoantibodies bind directly to syncytiotrophoblast and inhibit placental tissue transglutaminase activity. *Reprod. Biol. Endocrinol.* **2009**, *7*, 16. [[CrossRef](#)] [[PubMed](#)]
24. Barone, M.V.; Troncone, R.; Auricchio, S. Gliadin Peptides as triggers of the proliferative and stress/innate immune response of the celiac small intestinal mucosa. *Int. J. Mol. Sci.* **2014**, *15*, 20518–20537. [[CrossRef](#)] [[PubMed](#)]
25. Schuppan, D.; Cicciocioppo, R. Coeliac disease and secondary autoimmunity. *Dig. Liver Dis.* **2002**, *34*, 13–15. [[CrossRef](#)] [[PubMed](#)]
26. Denham, J.M.; Hill, I.D. Celiac disease and autoimmunity: Review and controversies. *Curr. Allergy Asthma Rep.* **2013**, *13*, 347–353. [[CrossRef](#)] [[PubMed](#)]
27. Singh, M.; Wambua, S.; Lee, S.I.; Okoth, K.; Wang, Z.; Fazla, F.; Fayaz, A.; Eastwood, K.-A.; Nelson-Piercy, C.; Nirantharakumar, K.; et al. Autoimmune diseases and adverse pregnancy outcomes: An umbrella review. *Lancet* **2023**, *402*, S84. [[CrossRef](#)] [[PubMed](#)]

28. Ciacci, C.; Cirillo, M.; Auriemma, G.; Di Dato, G.; Sabbatini, F.; Mazzacca, G. Celiac disease and pregnancy outcome. *Obstet. Gynecol. Surv.* **1996**, *51*, 643–644. [\[CrossRef\]](#)
29. Tursi, A.; Giorgetti, G.; Brandimarte, G.; Elisei, W. Effect of gluten-free diet on pregnancy outcome in celiac disease patients with recurrent miscarriages. *Dig. Dis. Sci.* **2008**, *53*, 2925–2928. [\[CrossRef\]](#)
30. Sansotta, N.; Amirikian, K.; Guandalini, S.; Jericho, H. Celiac disease symptom resolution: Effectiveness of the gluten-free diet. *J. Pediatr. Gastroenterol. Nutr.* **2018**, *66*, 48–52. [\[CrossRef\]](#)
31. Saturni, L.; Ferretti, G.; Bacchetti, T. The gluten-free diet: Safety and nutritional quality. *Nutrients* **2010**, *2*, 00016–00034. [\[CrossRef\]](#)
32. Rajpoot, P.; Makharia, G.K. Problems and Challenges to Adaptation of Gluten Free Diet by Indian Patients with Celiac Disease. *Nutrients* **2013**, *5*, 4869–4879. [\[CrossRef\]](#) [\[PubMed\]](#)
33. Marciniak, M.; Szymczak-Tomczak, A.; Mahadea, D.; Eder, P.; Dobrowolska, A.; Krela-Kaźmierczak, I. Multidimensional disadvantages of a gluten-free diet in celiac disease: A narrative review. *Nutrients* **2021**, *13*, 643. [\[CrossRef\]](#)
34. Agarwal, A.; Singh, A.; Mehtab, W.; Gupta, V.; Chauhan, A.; Rajput, M.S.; Singh, N.; Ahuja, V.; Makharia, G.K. Patients with celiac disease are at high risk of developing metabolic syndrome and fatty liver. *Intest. Res.* **2021**, *19*, 106–114. [\[CrossRef\]](#) [\[PubMed\]](#)
35. Shah, S.; Akbari, M.; Vanga, R.; Kelly, C.P.; Hansen, J.; Theethira, T.; Tariq, S.; Dennis, M.; Leffler, D.A. Patient perception of treatment burden is high in celiac disease compared with other common conditions. *Am. J. Gastroenterol.* **2014**, *109*, 1304–1311. [\[CrossRef\]](#) [\[PubMed\]](#)
36. Van Megen, F.; Fossli, M.; Skodje, G.I.; Carlsen, M.H.; Andersen, L.F.; Veierød, M.B.; Lundin, K.E.A.; Henriksen, C. Nutritional assessment of women with celiac disease compared to the general population. *Clin. Nutr. ESPEN* **2023**, *54*, 251–257. [\[CrossRef\]](#) [\[PubMed\]](#)
37. Maniero, D.; Lorenzon, G.; Marsilio, I.; D’odorico, A.; Savarino, E.V.; Zingone, F. Assessment of Nutritional Status by Bioelectrical Impedance in Adult Patients with Celiac Disease: A Prospective Single-Center Study. *Nutrients* **2023**, *15*, 2686. [\[CrossRef\]](#) [\[PubMed\]](#)
38. Maqbool, A.; Olsen, I.E.; Stallings, V. Clinical assessment of Nutritional Status. In *Nutrition in Pediatrics: Basic Science and Clinical Applications*, 4th ed.; BC Decker: Hamilton, ON, USA, 2008; pp. 6–7.
39. Soriano-Moreno, D.R.; Dolores-Maldonado, G.; Benites-Bullón, A.; Ccami-Bernal, F.; Fernandez-Guzman, D.; Esparza-Varas, A.L.; Caira-Chuquineyra, B.; Taype-Rondan, A. Recommendations for nutritional assessment across clinical practice guidelines: A scoping review. *Clin. Nutr. ESPEN* **2022**, *49*, 201–207. [\[CrossRef\]](#) [\[PubMed\]](#)
40. Morrison, J.L.; Regnault, T.R.H. Nutrition in Pregnancy: Optimising Maternal Diet and Fetal Adaptations to Altered Nutrient Supply. *Nutrients* **2016**, *8*, 342. [\[CrossRef\]](#)
41. Alecsandru, D.; Lopez-Palacios, N.; Castano, M.; Aparicio, P.; Garcia-Velasco, J.A.; Nunez, C. Exploring undiagnosed celiac disease in women with recurrent reproductive failure: The gluten-free diet could improve reproductive outcomes. *Am. J. Reprod. Immunol.* **2020**, *83*, e13209. [\[CrossRef\]](#)
42. Ayoub, A.; Firwana, M.; Amjahdi, A.; Rahaoui, A.; Benelbarhdadi, I.; Zahra, A.F. Evolution of Reproductive Disorders Related to Celiac Disease under Gluten-free Diet. *Int. J. Celiac Dis.* **2017**, *5*, 69–71. [\[CrossRef\]](#)
43. Kvamme, J.-M.; Sørbye, S.; Florholmen, J.; Halstensen, T.S. Population-based screening for celiac disease reveals that the majority of patients are undiagnosed and improve on a gluten-free diet. *Sci. Rep.* **2022**, *12*, 12647. [\[CrossRef\]](#) [\[PubMed\]](#)
44. Theethira, T.G.; Dennis, M.; Leffler, D.A. Nutritional consequences of celiac disease and the gluten-free diet. *Expert. Rev. Gastroenterol. Hepatol.* **2014**, *8*, 123–129. [\[CrossRef\]](#)
45. Aaron, L.; Patricia, W.; Ajay, R.; Torsten, M. Celiac disease and lactose intolerance. *Int. J. Celiac Dis.* **2018**, *6*, 68–70.
46. Jain, D.; Khuteta, R.; Chaturvedi, V.; Khuteta, S. Effect of body mass index on pregnancy outcomes in nulliparous women delivering singleton babies: Observational study. *J. Obstet. Gynecol. India* **2012**, *62*, 429–431. [\[CrossRef\]](#) [\[PubMed\]](#)
47. Cheng, J.; Brar, P.S.; Lee, A.R.; Green, P.H. Body mass index in celiac disease: Beneficial effect of a gluten-free diet. *J. Clin. Gastroenterol.* **2010**, *44*, 267–271. [\[CrossRef\]](#)
48. Mijatov, M.A.K.; Mičetić-Turk, D. Dietary intake in adult female coeliac disease patients in Slovenia. *Slov. J. Public. Health* **2016**, *55*, 96–103. [\[CrossRef\]](#) [\[PubMed\]](#)
49. Gessaroli, M.; Frazzoni, L.; Sikandar, U.; Bronzetti, G.; Pession, A.; Zagari, R.M.; Fuccio, L.; Forchielli, M.L. Nutrient intakes in adult and pediatric coeliac disease patients on gluten-free diet: A systematic review and meta-analysis. *Eur. J. Clin. Nutr.* **2023**, *77*, 784–793. [\[CrossRef\]](#) [\[PubMed\]](#)
50. Most, J.; Dervis, S.; Haman, F.; Adamo, K.B.; Redman, L.M. Energy Intake Requirements in Pregnancy. *Nutrients* **2019**, *11*, 1812. [\[CrossRef\]](#)
51. Meyers, L.D.; Hellwig, J.P.; Otten, J.J. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements*; National Academies Press: Washington, DC, USA, 2006.
52. Butte, N.F.; King, J.C. Energy requirements during pregnancy and lactation. *Public. Health Nutr.* **2005**, *8*, 1010–1027. [\[CrossRef\]](#)
53. Hytten, F.; Chamberlain, G. *Clinical Physiology in Obstetrics*; Blackwell Scientific Publications: Oxford, UK, 1991; pp. 150–172.
54. Capristo, E.; Addolorato, G.; Mingrone, G.; De Gaetano, A.; Greco, A.V.; A Tataranni, P.; Gasbarrini, G. Changes in body composition, substrate oxidation, and resting metabolic rate in adult celiac disease patients after a 1-y gluten-free diet treatment. *Am. J. Clin. Nutr.* **2000**, *72*, 76–81. [\[CrossRef\]](#)
55. Faisal, M.; Russell, L.; Collins, A.W.; Armstrong, D.; I Pinto-Sanchez, M. A255 Increased energy expenditure and reduced exercise capacity in celiac disease patients on a gluten-free diet. *J. Can. Assoc. Gastroenterol.* **2022**, *5* (Suppl. S1), 149–150. [\[CrossRef\]](#)

56. Bogin, B.; Varela-Silva, M.I. The body mass index: The good, the bad, and the horrid. *Bull Soc Suisse Anthr.* **2012**, *18*, 5–11.
57. Stephenson, J.; Heslehurst, N.; Hall, J.; Schoenaker, D.A.J.M.; Hutchinson, J.; Cade, J.E.; Poston, L.; Barrett, G.; Crozier, S.R.; Barker, M.; et al. Before the beginning: Nutrition and lifestyle in the preconception period and its importance for future health. *Lancet* **2018**, *391*, 1830–1841. [[CrossRef](#)]
58. Kabbani, T.A.; Goldberg, A.; Kelly, C.P.; Pallav, K.; Tariq, S.; Peer, A.; Hansen, J.; Dennis, M.; Leffler, D.A. Body mass index and the risk of obesity in coeliac disease treated with the gluten-free diet. *Aliment. Pharmacol. Ther.* **2012**, *35*, 723–729. [[CrossRef](#)] [[PubMed](#)]
59. Rasmussen, K.M.; Yaktine, A.L. *Weight Gain during Pregnancy: Reexamining the Guidelines*; National Academies Press (US): Washington, DC, USA, 2009.
60. A Brion, M.-J.; Ness, A.R.; Rogers, I.; Emmett, P.; Cribb, V.; Smith, G.D.; A Lawlor, D. Maternal macronutrient and energy intakes in pregnancy and offspring intake at 10 y: Exploring parental comparisons and prenatal effects. *Am. J. Clin. Nutr.* **2010**, *91*, 748–756. [[CrossRef](#)]
61. Lowensohn, R.I.; Stadler, D.D.; Naze, C. Current concepts of maternal nutrition. *Obstet. Gynecol. Surv.* **2016**, *71*, 413–426. [[CrossRef](#)]
62. Seal, C.J.; Courtin, C.M.; Venema, K.; de Vries, J. Health benefits of whole grain: Effects on dietary carbohydrate quality, the gut microbiome, and consequences of processing. *Compr. Rev. Food Sci. Food Saf.* **2021**, *20*, 2742–2768. [[CrossRef](#)] [[PubMed](#)]
63. Niro, S.; D’agostino, A.; Fratianni, A.; Cinquanta, L.; Panfili, G. Gluten-free alternative grains: Nutritional evaluation and bioactive compounds. *Foods* **2019**, *8*, 208. [[CrossRef](#)]
64. Martin, J.; Geisel, T.; Maresch, C.; Krieger, K.; Stein, J. Inadequate nutrient intake in patients with celiac disease: Results from a German dietary survey. *Digestion* **2013**, *87*, 240–246. [[CrossRef](#)]
65. Serin, Y.; Akbulut, G. Nutritional status and health-related quality of life in adult patients with celiac disease. *CBU Int. Conf. Proc.* **2018**, *6*, 952–959. [[CrossRef](#)]
66. Hall, N.J.; Rubin, G.; Charnock, A. Systematic review: Adherence to a gluten-free diet in adult patients with coeliac disease. *Aliment. Pharmacol. Ther.* **2009**, *30*, 315–330. [[CrossRef](#)] [[PubMed](#)]
67. Clapp, J.F., III. Maternal carbohydrate intake and pregnancy outcome. *Proc. Nutr. Soc.* **2002**, *61*, 45–50. [[CrossRef](#)] [[PubMed](#)]
68. Castellanos-Sinco, H.; Ramos-Peñafiel, C.; Santoyo-Sánchez, A.; Collazo-Jaloma, J.; Martínez-Murillo, C.; Montaña-Figueroa, E.; Sinco-Ángeles, A. Megaloblastic anaemia: Folic acid and vitamin B12 metabolism. *Rev. Médica Del Hosp. Gen. De México* **2015**, *78*, 135–143. [[CrossRef](#)]
69. Schrott, R.; Murphy, S.K. Folic acid throughout pregnancy: Too much? *Am. J. Clin. Nutr.* **2018**, *107*, 497–498. [[CrossRef](#)] [[PubMed](#)]
70. Di Nardo, G.; Villa, M.P.; Conti, L.; Ranucci, G.; Pacchiarotti, C.; Principessa, L.; Raucci, U.; Parisi, P. Nutritional deficiencies in children with celiac disease resulting from a gluten-free diet: A systematic review. *Nutrients* **2019**, *11*, 1588. [[CrossRef](#)] [[PubMed](#)]
71. Trumbo, P.; Yates, A.A.; Schlicker, S.; Poos, M. Dietary reference intakes: Vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. *J. Am. Diet. Assoc.* **2001**, *101*, 294–301. [[CrossRef](#)] [[PubMed](#)]
72. European Food Safety Authority (EFSA). *Dietary Reference Values for Nutrients Summary Report*; Wiley Online Library: Minneapolis, MN, USA, 2017.
73. Scholl, T.O.; Reilly, T. Anemia, Iron and pregnancy outcome. *J. Nutr.* **2000**, *130*, 443S–447S. [[CrossRef](#)]
74. Dainty, J.R.; Berry, R.; Lynch, S.R.; Harvey, L.J.; Fairweather-Tait, S.J. Estimation of dietary iron bioavailability from food iron intake and iron status. *PLoS ONE* **2014**, *9*, e111824. [[CrossRef](#)]
75. Montoro-Huguet, M.A.; Santolaria-Piedrafita, S.; Cañamares-Orbis, P.; García-Erce, J.A. Iron deficiency in celiac disease: Prevalence, health impact, and clinical management. *Nutrients* **2021**, *13*, 3437. [[CrossRef](#)]
76. Institute of Medicine (US) Panel on Micronutrients. *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc*. Institute of Medicine/Food and Nutrition Board; National Academy Press: Washington, DC, USA, 2001.
77. Jouanne, M.; Oddoux, S.; Noël, A.; Voisin-Chiret, A.S. Nutrient requirements during pregnancy and lactation. *Nutrients* **2021**, *13*, 692. [[CrossRef](#)] [[PubMed](#)]
78. Willemse, J.P.M.M.; Meertens, L.J.E.; Scheepers, H.C.J.; Achten, N.M.J.; Eussen, S.J.; van Dongen, M.C.; Smits, L.J.M. Calcium intake from diet and supplement use during early pregnancy: The Expect study I. *Eur. J. Nutr.* **2020**, *59*, 167–174. [[CrossRef](#)] [[PubMed](#)]
79. World and Health Organization. *Guideline: Calcium Supplementation in Pregnant Women*; World Health Organization: Geneva, Switzerland, 2013.
80. FAO/WHO. *Human Vitamin and Mineral Requirements: Report of a Joint FAO/WHO Expert Consultation Bangkok, Thailand Food and Nutrition Division*; FAO: Rome, Italy, 2001.
81. Zanchetta, M.B.; Longobardi, V.; Bai, J.C. Bone and celiac disease. *Curr. Osteoporos. Rep.* **2016**, *14*, 43–48. [[CrossRef](#)] [[PubMed](#)]
82. Grace-Farfaglia, P. Bones of contention: Bone mineral density recovery in celiac disease—A systematic review. *Nutrients* **2015**, *7*, 3347–3369. [[CrossRef](#)]
83. Urrutia, R.P.; Thorp, J.M. Vitamin D in pregnancy: Current concepts. *Curr. Opin. Obstet. Gynecol.* **2012**, *24*, 57. [[CrossRef](#)] [[PubMed](#)]

84. Lerner, A.; Shapira, Y.; Agmon-Levin, N.; Pacht, A.; Shor, D.B.-A.; López, H.M.; Sanchez-Castanon, M.; Shoenfeld, Y. The clinical significance of 25OH-Vitamin D status in celiac disease. *Clin. Rev. Allergy Immunol.* **2012**, *42*, 322–330. [CrossRef]
85. Perichart-Perera, O.; Rodríguez-Cano, A.M. Micronutrient supplementation during pregnancy: Narrative review of systematic reviews and meta-analyses. *Ginecol. Y Obstet. De México* **2023**, *90*, 968–994.
86. Institute of Medicine (US) Committee to Review Dietary Reference Intakes for Vitamin D and Calcium. *Dietary Reference Intakes for Calcium and Vitamin D*; Ross, A.C., Taylor, C.L., Yaktine, A.L., Del Valle, H.B., Eds.; National Academies Press (US): Washington, DC, USA, 2011.
87. O’Leary, F.; Samman, S. Vitamin B12 in health and disease. *Nutrients* **2010**, *2*, 299–316. [CrossRef] [PubMed]
88. Molloy, A.M.; Kirke, P.N.; Troendle, J.F.; Burke, H.; Sutton, M.; Brody, L.C.; Scott, J.M.; Mills, J.L. Maternal vitamin B12 status and risk of neural tube defects in a population with high neural tube defect prevalence and no folic acid fortification. *Pediatrics* **2009**, *123*, 917–923. [CrossRef]
89. Caruso, R.; Pallone, F.; Stasi, E.; Romeo, S.; Monteleone, G. Appropriate nutrient supplementation in celiac disease. *Ann. Med.* **2013**, *45*, 522–531. [CrossRef]
90. Wierdsma, N.J.; van Bokhorst-de van der Schueren, M.A.E.; Berkenpas, M.; Mulder, C.J.J.; van Bodegraven, A.A. Vitamin and mineral deficiencies are highly prevalent in newly diagnosed celiac disease patients. *Nutrients* **2013**, *5*, 3975–3992. [CrossRef] [PubMed]
91. Brown, B.; Wright, C. Safety and efficacy of supplements in pregnancy. *Nutr. Rev.* **2020**, *78*, 813–826. [CrossRef] [PubMed]
92. Garner, C. Nutrition in Pregnancy: Dietary Requirements and Supplements. Available online: https://www.uptodate.com/contents/nutrition-in-pregnancy-dietary-requirements-and-supplements?sectionName=Iron&search=clinical-presentation-anddiagnosis-of-von-willebrand-disease&topicRef=7150&anchor=H717781762&source=see_link (accessed on 19 April 2023).
93. U.S. Food and Drug Administration (FDA). *Questions and Answers on Dietary Supplements*. Available online: <https://www.fda.gov/food/information-consumers-using-dietary-supplements/questions-and-answers-dietary-supplements> (accessed on 7 July 2024).
94. EFSA NDA Panel (EFSA Panel on Nutrition, Novel Foods and Food Allergens); Turck, D.; Bohn, T.; Castenmiller, J.; De Henauw, S.; Hirsch-Ernst, K.I.; Knutsen, H.K.; Maciuk, A.; Mangelsdorf, I.; McArdle, H.J.; et al. Guidance for establishing and applying tolerable upper intake levels for vitamins and essential minerals. *EFSA J.* **2022**, *20*, 1–27.
95. Belkacemi, L.; Nelson, D.M.; Desai, M.; Ross, M.G. Maternal undernutrition influences placental-fetal development1. *Biol. Reprod.* **2010**, *83*, 325–331. [CrossRef] [PubMed]
96. Mehta, N.M.; Skillman, H.E.; Irving, S.Y.; Coss-Bu, J.A.; Vermilyea, S.; Farrington, E.A.; McKeever, L.; Hall, A.M.; Goday, P.S.; Braunschweig, C. Guidelines for the provision and assessment of nutrition support therapy in the pediatric critically ill patient: Society of critical care medicine and American society for parenteral and enteral nutrition. *J. Parenter. Enter. Nutr.* **2017**, *41*, 706–742. [CrossRef] [PubMed]
97. Mihatsch, W.A.; Braegger, C.; Bronsky, J.; Cai, W.; Campoy, C.; Carnielli, V.; Darmaun, D.; Desci, T.; Domellof, M.; Embleton, N.; et al. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition. *Clin. Nutr.* **2018**, *37*, 2303–2305. [CrossRef] [PubMed]
98. Fewtrell, M.; Bronsky, J.; Campoy, C.; Domellöf, M.; Embleton, N.; Mis, N.F.; Hojsak, I.; Hulst, J.M.; Indrio, F.; Lapillonne, A.; et al. Complementary feeding: A position paper by the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) Committee on Nutrition. *J. Pediatr. Gastroenterol. Nutr.* **2017**, *64*, 119–132. [CrossRef] [PubMed]
99. Hill, I.D.; Fasano, A.; Guandalini, S.; Hoffenberg, E.; Levy, J.; Reilly, N.; Verma, R. NASPGHAN clinical report on the diagnosis and treatment of gluten-related disorders. *J. Pediatr. Gastroenterol. Nutr.* **2016**, *63*, 156–165. [CrossRef] [PubMed]
100. Shivakumar, N.; Jackson, A.A.; Courtney-Martin, G.; Elango, R.; Ghosh, S.; Hodgkinson, S.; Xipsiti, M.; Lee, W.T.; Kurpad, A.V.; Tomé, D. Protein quality assessment of follow-up formula for young children and ready-to-use therapeutic foods: Recommendations by the FAO expert. working group. in 2017. *J. Nutr.* **2020**, *150*, 195–201. [CrossRef]
101. WHO. *The International Code of Marketing of Breast-Milk Substitutes: Frequently Asked Questions*; World Health Organization: Geneva, Switzerland, 2017.
102. Hojsak, I.; Chourdakis, M.; Gerasimidis, K.; Hulst, J.; Huysentruyt, K.; Moreno-Villares, J.M.; Joosten, K. What are the new guidelines and position papers in pediatric nutrition: A 2015–2020 overview. *Clin. Nutr. ESPEN* **2021**, *43*, 49–63. [CrossRef]
103. Romano, C.; van Wynckel, M.; Hulst, J.; Broekaert, I.; Bronsky, J.; Dall’Oglio, L.; Mis, N.F.; Hojsak, I.; Orel, R.; Papadopoulou, A.; et al. European society for paediatric gastroenterology, hepatology and nutrition guidelines for the evaluation and treatment of gastrointestinal and nutritional complications in children with neurological impairment. *J. Pediatr. Gastroenterol. Nutr.* **2017**, *65*, 242–264. [CrossRef] [PubMed]
104. Mouzaki, M.; Bronsky, J.; Gupta, G.; Hojsak, I.; Jahnel, J.; Pai, N.; Quiros-Tejeira, R.E.; Wieman, R.; Sundaram, S. Nutrition support of children with chronic liver diseases: A joint position paper of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. *J. Pediatr. Gastroenterol. Nutr.* **2019**, *69*, 498–511. [CrossRef] [PubMed]
105. Raiteri, A.; Granito, A.; Giamperoli, A.; Catenaro, T.; Negrini, G.; Tovoli, F. Current guidelines for the management of celiac disease: A systematic review with comparative analysis. *World J. Gastroenterol.* **2022**, *28*, 154–176. [CrossRef] [PubMed]

106. Husby, S.; Koletzko, S.; Kurppa, K.; Mearin, M.L.; Shamir, R.; Troncone, R.; Auricchio, R.; Castillejo, G.; Christensen, R.; Dolinsek, J.; et al. European society paediatric gastroenterology, hepatology and nutrition guidelines for diagnosing coeliac disease 2020. *J. Pediatr. Gastroenterol. Nutr.* **2020**, *70*, 141–156. [[CrossRef](#)]
107. Mearin, M.L.; Agardh, D.; Antunes, H.; Al-Toma, A.; Auricchio, R.; Castillejo, G.; Catassi, C.; Ciacci, C.; Discepolo, V.; Dolinsek, J.; et al. ESPGHAN position paper on management and follow-up of children and adolescents with celiac disease. *J. Pediatr. Gastroenterol. Nutr.* **2022**, *75*, 369–386. [[CrossRef](#)]

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