Dietary Recommendations for Twin Pregnancy

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Recommendations for nutrition and the use of dietary supplements for pregnant women are updated on regular basis but it remains to be seen to what extent they may be applicable in twin pregnancies. Over the past 30 years, there has been a considerable increase in the number of multiple pregnancies worldwide, which mainly applies to dizygotic pregnancies. In the USA, in 2009 compared to the 1980s, the number of twin pregnancies increased by 76%; the situation was similar in Australia (66%). A multiple pregnancy is associated with an increased risk of its abnormal course. This mostly applies to pre-eclampsia, hypertension, diabetes, iron-deficiency anemia and pre-term birth that affects 50–60% of twin pregnancies.

Keywords: twin pregnancy ; nutrition ; requirements ; supplementation ; pregnancy outcomes

1. Introduction

Over the past 30 years, there has been a considerable increase in the number of multiple pregnancies worldwide, which mainly applies to dizygotic pregnancies. In the USA, in 2009 compared to the 1980s, the number of twin pregnancies increased by 76%; the situation was similar in Australia (66%) [1][2]. Currently, it is estimated that in the United States, twin births account for 3.0–3.5% of all births (one twin birth out of approx. 30 births), much like in France and Australia—more than 3%. A lower proportion is observed in Central Africa (1.8%) and Great Britain (1.5%), while in East Asia and Oceania, the incidence of twin pregnancies has been stable over the years and amounts to <1% of all births [2][3][4][5][6][7][8][9]. This upward trend has also been observed in Poland. According to the Yearbook of Statistics Poland, in 1990, twin pregnancies accounted for 1% of all births, while in 2018, 1.3%, which corresponds to 4925 births [10][11].

Among the reasons for the increased number of multiple pregnancies, several factors are taken into consideration. The main one is the use of assisted reproductive technology, which is probably responsible for two-thirds of said increase; the other is the more advanced age of women giving birth, which accounts for approximately one-quarter of the increase [9][12][13][14][15][16]. As an example, in 2002 in the USA, the number of twin pregnancies in women aged ≥ 40 was 11 times higher compared to 1980 [17]. In Poland, in 1990, twin pregnancies after the age of 35 constituted 11.5% of all twin pregnancies, while in 2018, it was 23.3% [10][11]. The mother's pre-pregnancy obesity can also be of considerable importance. It is estimated that with a *body mass index* (BMI) of >30, the risk of a twin pregnancy grows by 40%, which, in times of globally increasing obesity, can be an important factor conducive to multiple pregnancies [9][14][15][16]. Literature also investigates pre-pregnancy folic acid use and mandatory folic acid food fortification introduced in many countries [2][18][19][20].

A multiple pregnancy is associated with an increased risk of its abnormal course. This mostly applies to pre-eclampsia, hypertension, diabetes, iron-deficiency anemia and pre-term birth that affects 50–60% of twin pregnancies. For newborns, the risk mainly concerns low birth weight (<2500 g) and the resulting perinatal death [6][13][21][22][23][24]. When it comes to twin pregnancies, low birth weight applies to approx. 50% newborns, a birth weight of <1500 g applies to 10%, while for newborns from a singleton pregnancy, it is 6% and 1%, respectively [15].

Although nutritional recommendations for pregnant women are quite detailed and do not specify the type of pregnancy [25][26][27], these refer to women who expect one baby by default. For multiple pregnancies, literature shows a clear gap in knowledge and, thereby, a lack of separate guidelines. Actually, multiple pregnancies are rarely the subject matter of scientific studies. An estimation of the number of randomized studies carried out in the years 2012–2016 with regard to pregnancy complications demonstrates that, in reference to fetal growth restriction, gestational diabetes and pre-eclampsia, there is not one study concerned with multiple pregnancies only. A slightly better situation is seen for studies associated with pre-term birth, where out of all the studies, 18% applied to multiple pregnancies, while 17% to multiple and singleton pregnancies together [13].

2. Energy Requirement of Women Pregnant with Twins

Energy requirement in pregnancy is defined as a dietary energy value needed to provide the optimum development of maternal tissue and fetal growth [28]. Pregnancy increases resting energy expenditure due to the development of the placenta and the fetus as well as the enhanced maternal heart and lung function [29]. Basal metabolic rate in women with a singleton pregnancy increases by approx. 5% in the first trimester of pregnancy, by 11% in the second trimester and 24% in the third trimester [30][31]. When it comes to a twin pregnancy, scientific data suggest that, in the third trimester, basal metabolic rate increases by additional 10%. Apart from energy expenditure by the mother's body, the total energy requirement also includes the accumulation of energy in the form of fatty tissue, referred to as energy storage [32].

The diet's energy value determines the gestational body weight gain [15][33]. According to expert guidelines from the Food and Agriculture Organization, World Health Organization and United Nations University (FAO/WHO/UNU), standards for singleton pregnancies assume that the normal body weight gain is on average 12 kg. In such a case, the overall energy cost of pregnancy is estimated at 77,000 kcal (on average 275 kcal per day) and this additional energy should be properly distributed over the individual trimesters of pregnancy [30]. The worldwide recommendations for energy intake in singleton pregnancies are quite similar. According to guidelines from North America, Europe, Australia and New Zealand, the higher energy requirement starts from the second trimester (by 335–360 kcal/day) to reach 450–475 kcal in the third trimester. Only Japan recommends a small increase of 50 kcal already in the first trimester, while in the subsequent trimesters, it is 250 and 500 kcal/day higher, respectively [34].

In terms of a twin pregnancy, there is general consensus in literature that, due to the higher weight of maternal tissues, the development of two fetuses and increased energy expenditure, the energy requirement is even larger [14][15][33]. It needs to be noted, however, that due to a lack of studies, these are only theoretical assumptions, and the actual energy needs of women pregnant with twins remain unknown [14][17]. Taking the target body weight gain of 20 kg in women with a twin pregnancy, some estimate that throughout the entire pregnancy, additional 35,000 kcal need to be supplied in excess of what is already needed for a singleton pregnancy. Considering the higher restrictions in physical activity, this means that 150 kcal need to be additionally consumed per day compared to the recommendations for singleton pregnancies [14][15]. Gandhi et al., in their study among women with a dichorionic diamniotic twin pregnancy, estimated that up until 30–32 weeks of gestation, weight gain comprised about 6 kg of fat mass and 2 kg of protein, equal to a mean energy deposition of 67,042 kcal. The third trimester energy requirement estimated by the authors increased by 29% compared to the first trimester—from 2257 ± 325 kcal/d in the first trimester to 2906 ± 350 kcal/d in the third trimester [33]. The authors argue that, in order to cover the increased energy expenditure and ensure the normal maternal body weight gain, the energy intake in women pregnant with twins should grow by an average of 700 kcal daily in the second and third trimester compared to the first trimester. On the other hand, the results of the Canadian *Higgins Nutrition Intervention Program* indicate that, after the 20th week of pregnancy, it is advisable to consume additional 1000 calories per day and 50 g of protein (by convention, 500 kcal and 25 g of protein per each child) compared to women who are not pregnant. Such a diet resulted in the increased body weight of the twins by an average of 80 g and the reduced number of pre-term births by 30%, compared to the twins of mothers from the control group [35].

Analogically, as in a singleton pregnancy, the diet's energy value should be adapted to the mother's pre-pregnancy BMI. Luke reports that the energy requirement in preconceptionally underweight women pregnant with twins amounts to 4000 kcal, in women with normal pre-pregnancy weight—3500 kcal, in overweight women—3250 kcal, while in obese women—3000 kcal [17]. Similar values are given by Whitaker et al., who claim that women with normal pre-pregnancy BMI need 3000–3500 kcal, overweight women—3250 kcal and obese women—2700–3000 kcal [7], while in the light of the guidelines from the Alberta Health Services, the diet's energy value in a twin pregnancy should amount to 3000–4000 kcal, with the lowest value applying to women with an excessive preconceptional BMI and the highest to slim women [36]. A different group of experts claims that women pregnant with twins with a normal pre-pregnancy body weight need 40–45 kcal/kg bw/day in the first trimester, with a possible modification in the next trimesters, in order to ensure the normal maternal body weight gain [37]. Based on this premise, assuming the body weight of a mother-to-be is, for example, 70 kg, this would mean that her diet in the first trimester should amount to 2800–3150 kcal per day.

Just like in singleton pregnancies, determining the optimum energy value of the diet presents a particular challenge in obese women who are at risk of an excessive body weight gain. At the moment, there is a lack of studies among women pregnant with twins, but, based on studies among women with a singleton pregnancy, it can be deliberated whether or not a small energy deficit in the diet might be an effective solution preventing an excessive body weight gain. One of such studies demonstrated that the normal body weight gain in women with pre-pregnancy obesity was achieved when the diet's energy value was on average 125 kcal/day lower than the body's energy expenditure, while the consumption of 186 kcal more compared to the energy expenditure led to an excessive body weight gain. The authors of said study therefore

recommend that the energy value of the diet of pregnant women with obesity should not exceed the body's total energy expenditure [38]. An estimation of pregnant women's energy requirements carried out by Most et al., show that in order to achieve the normal body weight gain, obese women not only should stop accumulating energy in the form of fatty tissue, but should even derive approximately 160 kcal from their body's energy stores per day. In practice, it means supplying 5% less energy with the diet compared to the energy expenditure [28]. Given that energy accumulated during pregnancy in the form fatty tissue is to serve as an energy reserve for the postpartum period and lactation and that in countries not affected by the problem of starvation and access to food, it seems that overweight women pregnant with twins should not store energy in the form of fatty tissue because energy stores in the body are sufficient for the pregnancy and subsequent lactation.

At this point, it is worth citing a very interesting study concerned with dietary advice for American women pregnant with twins. It demonstrated that only 30% women received recommendations regarding the diet's calorie value. Among them, 6.4% stated that they were told to consume 300–500 kcal/day more, while 4.6% women said that an additional 600–1500 kcal were recommended. Further 8.1% women were advised that the total energy value of their diet should amount to 2500–3500 kcal per day; other recommended values were 2000–2500 kcal (4.6% women) and 1600–1800 kcal (2.3% women) [7]. This shows very diverse approaches adopted by dieticians and the complexity of this problem.

It needs to be acknowledged that women pregnant with twins suffer from nausea, vomiting and early satiety much more often than women with a singleton pregnancy, which can cause difficulties in adhering to the higher requirements [36][39][40]. A study by Morley et al., demonstrates that the median of daily energy intake by women pregnant with twins at 29–35 weeks of gestation ranged from 2363 to 2388 kcal [41]. Theoretically, it would indicate an energy deficit in the diet, which actually should not come as a surprise because energy intake considerably lower than the guidelines is commonly observed in singleton pregnancies as well. In the light of a 2012 meta-analysis of observational studies, average energy intake in pregnancy in the USA and Canada amounted to 2199 kcal, in Europe—2194 kcal, while in Japan only 1839 kcal [34]. Similar results were obtained in a meta-analysis of 2016, where average energy intake was 1940 kcal/day in the first trimester and 2052 kcal/day in the third trimester [42].

3. Vitamin Requirement

Many experts claim that the requirement for vitamins and minerals is higher in a twin pregnancy than it is in a singleton pregnancy, but it is not currently established and this view is based on a hypothesis that the maternal body reserves are used up faster [14][15][17][37][39][43]. For most vitamins and minerals, there either no studies that would assess their concentration in the body of a woman pregnant with twins or there are very few such studies (**Table 1** summarizes the studies included in this entry). First of all, there are no randomized studies relating to the effects of dietary interventions on the course of pregnancy, which means there are no grounds for reliable guidelines as regards vitamin and mineral intake and dietary supplementation [4][7][13][44]. The only dietary supplementation guidelines for women pregnant with twins known to the author were published in 1990 by the American Institute of Medicine and Alberta Health Services in Canada (2018) [14][36].

Table 1. Characteristics of studies on the concentration of nutrients and their supplementation in women pregnant with twins.

Authors	Study Design	Participants	Type of Nutrients	Duration of the Study	Results
Corsi et al., 2020 [45]	Randomized Controlled Trial	428 women with twin pregnancy	Folic acid (4.0–5.1 mg vs. placebo)	II–III trimester of pregnancy	No effect of a high dose of folic acid in the prevention of pre-eclampsia
Wen et al., 2018 [46]	Randomized Controlled Trial	2464 women with singleton or twin pregnancies	Folic acid (4.0 mg vs. placebo)	From 8 weeks of pregnancy to delivery	No effect of a high dose of folic acid in the prevention of pre-eclampsia
Zhang et al., 2020 [47]	Cross-sectional study	28,174 women with singleton or twin pregnancies	Folic acid (0.4 mg)	From 12 weeks before pregnancy to the end of the first trimester of pregnancy	15–55% reduction in small-for-gestational-age infant. 18–50% reduction in low birth weight infant. Increased birth weight by 17.3–166.3 g

Authors	Study Design	Participants	Type of Nutrients	Duration of the Study	Results
Nakayama et al., 2011 [48]	Cross-sectional study	322 women with singleton or twin pregnancies	Vitamin D, calcium	From 10 to 36 weeks of pregnancy	Concentration of $1,25(OH)_2D$ and 25(OH)D in women with twin pregnancy were lower than in women with singleton pregnancy. Serum calcium concentration in women with twin in the 25th and 30th week of pregnancy were higher than in women with singleton pregnancy. Concentration of bone resorption markers in women with twin pregnancy were higher than in women with singleton pregnancy
Goswami et al., 2016 [44]	Cross-sectional study	100 women with singleton or twin pregnancies	Vitamin D, calcium	Time of childbirth	Concentration of 25(OH)D and calcium in women with twin pregnancy were lower than in women with singleton pregnancy
Li et al., 2021 [49]	Prospective subcohort study	72 women with twin pregnancy	Vitamin D	III trimester of pregnancy	Twin neonates were at high risk of vitamin D deficiency
Bodnar et al., 2013 [43]	Cohort study	661 women with twin pregnancy	Vitamin D	From 24 to 28 weeks of pregnancy	60% reduction in preterm birth (< 35 weeks of pregnancy) at a concentration of 25(OH)D ≥ 30 ng/mL compared to a concentration < 30 ng/mL
Okah et al., 1996 [50]	Cross-sectional study	47 women with singleton or twin pregnancies	Vitamin D	III trimester of pregnancy	Concentration of 25(OH)D in women with twin pregnancy were higher than in women with singleton pregnancy. Concentration of bone resorption markers in women with twin pregnancy were higher than in women with singleton pregnancy
Shinar et al., 2017 [51]	Randomized Controlled Trial	172 iron-deficient women with twin pregnancy	Iron (34 mg of ferrous sulfate vs. 68 mg)	From 16 weeks of pregnancy to 6 weeks postpartum	The dose of 68 mg of elemental ferrous sulfate is beneficial for iron-deficient women with twin pregnancies
Ali et al., 2017 [52]	Randomized Controlled Trial	120 non-anemic women with twin pregnancy	Iron (27 mg elemental iron vs. 54 mg)	From 12 to 36 weeks of pregnancy	The effectiveness of the dose of 54 mg elemental iron and 27 mg is compared in the prevention of anemia
Abbas et.al., 2020 [53]	Randomized Controlled Trial	450 non-anemic women with twin pregnancy	Iron (27 mg elemental iron vs. 54 mg)	From 12 weeks of pregnancy to delivery	Compared to the single dose, the double supplemental iron dose has not significantly lowered the incidence of iron deficiency anemia, nor has contributed to increase of the hemoglobin concentration in pregnancies not complicated by iron deficiency anemia.

3.1. Folic Acid

Folic acid is an essential nutrient in pregnancy, which is more required, for example, due to the increased cell division process [2]. According to the American Institute of Medicine and European Food Safety Authority, the requirement for pregnant women is 600 µg/day [54]. Due to problems with covering this requirement by diet alone, global guidelines indicate it is necessary to supplement folic acid at a minimum of 400 µg per day [20]. It is estimated that the risk of folate-deficiency anemia in a twin pregnancy is eight times higher than in a singleton pregnancy [36], which raises the question of whether the requirements for a woman with a twin pregnancy are the same or higher and, possibly, how much higher than for women with a singleton pregnancy.

According to old 1990 guidelines from the Institute of Medicine, women pregnant with twins should take the same dose of folic acid as women with a singleton pregnancy, which is 300 µg [15]. It needs to be noted, though, it is a lower dose than the one recommended in the recent years to prevent neural tube defects. According to Canadian guidelines, women pregnant with twins should take in total 1000 µg of folic acid (from food and supplements) and should not exceed this amount on their own [36]. It is worth mentioning that the 1000 µg dose of folic acid is a dose referred to as Tolerable Upper

Intake Level (UL) for adults, including pregnant women [54]. The folic acid dose of 1000 µg per day for women with a twin pregnancy is also recommended by Goodnight et al. [37].

There are currently no data yet on the relationship between the folic acid intake/supplementation by women pregnant with twins and neural tube defects. However, statistical data indicate that the incidence of neural tube defects for twin pregnancies is higher than for singleton pregnancies and amounts to 2.3/1000 births [55]. In terms of folic acid supplementation, randomized controlled studies do not show any advantages of such a solution from the perspective of preventing pre-eclampsia (a frequent complication in twin pregnancies). In one of them, high doses of folic acid (4.0–5.1 mg daily) given to women pregnant with twins did not reduce the risk of this complication; in the treatment group, the incidence of pre-eclampsia was even higher than in the placebo group, although the differences found were not statistically significant [45]. In the other randomized study, no benefits were observed among women at a high risk of pre-eclampsia (including women pregnant with twins), who supplemented 4.0 mg folic acid/day [46]. Folic acid supplementation in pregnancy can also be associated with the newborns' birth weight, although data in that respect usually apply to singleton pregnancies only [56]. The only study known to the author that related to women with a twin pregnancy in China demonstrated that, in women taking 400 µg folic acid before pregnancy and in the first trimester of pregnancy, the risk of a small-for-gestational-age infant was 55% lower and the risk of low birth weight was 50% lower, compared to women who did not supplement this vitamin [47].

3.2. Vitamin D

It is believed that increased requirements and a higher risk of deficits in a twin pregnancy also applies to vitamin D [39][44], but due to insufficient studies on the actual requirements, the Institute of Medicine does not differentiate the recommended intake between singleton and twin pregnancies [57]. Although the scientific interest in vitamin D has been enormous in the recent years, it seems that, as opposed to other vitamins, the discussion here revolves more around its recommended blood concentration than its recommended intake. Considering the recommended serum 25(OH)D concentration proposed by some experts, which is at least 30 ng/mL, vitamin D deficiencies among pregnant women are common and apply to 99–100% women in Turkey [58], 69–95% in Central Europe [59][60], 52–85% in Southern Europe [61], 74% in the United States [62] and 63% in China [63].

Most studies indicate that vitamin D blood concentration in women with a multiple pregnancy is lower than in women with a singleton pregnancy. In Japanese women, throughout the entire pregnancy, the average 25(OH)D concentration in women pregnant with twins was considerably lower and, in the 36th week of pregnancy, amounted to 15.0 ng/mL as compared to 25.3 ng/mL in a singleton pregnancy [48]. In India, the average concentration in women pregnant with twins at birth was 5.7 ng/mL and, just like in the Japanese study, it was statistically significantly lower than in women with a singleton pregnancy (7.4 ng/mL). An analogical situation was observed for the infants' cord blood. The average vitamin D concentration in twins and singleton infants amounted to 5.9 ng/mL and 9.1 ng/mL, respectively. At this point, it is worth emphasizing that despite large vitamin D deficits, there is currently no recommendations in India relating to dietary supplementation in pregnant women, regardless of whether this is a singleton or twin pregnancy [44]. A higher 25(OH)D blood concentration in women with a multiple pregnancy compared to women with a singleton pregnancy has so far been observed in an American study only (61 ng/mL vs. 39 ng/mL) [50]. In China, in spite of the fact that the vitamin D concentration in mothers pregnant with twins was quite high (on average 31.8 ng/mL), which could arise from the fact that all the women took vitamin–mineral supplements containing vitamin D, the cord blood concentrations were considerably lower than the mothers' concentrations (on average 15.4 ng/mL) and as much as 78.5% of the newborns had vitamin D deficiency (concentration < 20 ng/mL) [49]. A study among American women with a twin pregnancy demonstrated that, although the mean 25(OH)D concentration was as high (33.1 ng/mL) as in the Chinese study, more than 40% of the women had less than 30 ng/mL of blood vitamin D. Compared to the vitamin D concentration below 30 ng/mL, concentration 30 ng/mL or above was associated with an 60% reduction in risk of preterm birth less than 35 weeks [43].

It is worth mentioning that the approach to vitamin D supplementation in pregnancy is very diverse on a global scale. According to the last consensus of world's scientific organizations (2016), pregnant women are advised to supplement 600 IU/day [64], although WHO's latest statement (2020) indicates that supplementation should only apply to women with suspected vitamin D deficiency and, in such a situation, the dose of 200 IU/day is sufficient [65]. The recommendations of the Polish Society of Gynecologists and Obstetricians subject the vitamin D dose to the patient's BMI. For women with a normal body weight, 1500–2000 IU/day of vitamin D is recommended, while for obese women—after consultation with a physician—a higher dose of 4000 IU [66]. None of the above recommendations specifically refer to women with a multiple pregnancy, with only Canada and the USA expressing their opinion on the supplementation of this vitamin by women pregnant with twins. Based on the Canadian guidelines from Alberta Health Services, such women should intake 1200 IU of vitamin D and should not exceed 4000 IU per day [36], while according to the recommendations of the American

Institute of Medicine, the dose of vitamin D should only amount to 200 IU [14]. Taking into account the currently common vitamin D deficiencies, the American guidelines seem to be questionable.

4. Mineral Requirement

4.1. Iron

Iron is an essential nutrient that is necessary for the normal course of pregnancy. It is estimated that, in a singleton pregnancy, the requirement for absorbed iron increases throughout the entire pregnancy by an average of 4.4 mg per day (0.8 mg per day at the beginning of pregnancy up to 7.5 mg in an advanced pregnancy) [67]. The European Food Safety Authority does not, however, recommend taking iron in excess of what is necessary for women who are not pregnant because in pregnancy, the absorption of this element is enhanced [68]. In a twin pregnancy, the iron requirement is 1.8 times higher compared to a singleton pregnancy. It stems from the additionally increased blood volume (by 10–20% compared to a singleton pregnancy), increased red blood count (up to the 20th week of pregnancy by 20–25% compared to a singleton pregnancy) and different needs of the mother and her children [15][69][51]. Anemia in women pregnant with twins occurs 2.4–4 times more frequently than in women with a singleton pregnancy and affects 30–45% of pregnant women in the third trimester [3][51][70]. Anemia in pregnancy is generally defined as a hemoglobin concentration below 11.0 g/dL in the first and third trimester of pregnancy and ≤10.5 g/dL in the second trimester [3], although according to some experts, the limit hemoglobin concentration in the third trimester is 10.5 g/dL [67][71]. Publications usually do not touch upon the issues of separate criteria for anemia in women pregnant with twins [72][73], but Shinar et al., suggest that in the second trimester, the cut-off point for hemoglobin concentration should be 9.7 g/dL because it is the best prognostic indicator for anemia [74].

It is commonly known that anemia in pregnancy increases the risk of pre-term birth and low birth weight [15][17][51][75][76]. It is estimated that, if anemia develops in women with a twin pregnancy at 12 weeks, the risk of pre-term birth increases to 29–68%, while if it happens at 16–18 weeks, the risk is three- to four-fold [77]. According to Luke, low hemoglobin concentrations lead to the adaptive enlargement of the placenta and can adversely affect the children's susceptibility to hypertension in the subsequent years of their life [77]. A randomized study among 87 Israeli women pregnant with twins suffering from iron-deficiency anemia demonstrated that, in women who took 68 mg of elemental iron from the 16th week of pregnancy to 6 weeks postpartum, the hemoglobin and ferritin concentrations at 32 weeks and postpartum were statistically significantly higher than in a group taking 34 mg of iron. Therefore, the authors claim that women with anemia should preferably take a double dose of iron, although the same authors, in a different study carried out among women with a singleton pregnancy, did not demonstrate that such a dose significantly increases the hemoglobin and ferritin concentrations. At the same time, a study among women with a twin pregnancy did not show any difference in the duration of pregnancy and the newborns' birth weight based on the iron dose [51]. The other randomized study was carried out in Egypt among 120 non-anemic women pregnant with twins in the first trimester who took 27 mg and 54 mg of elemental iron. It was found that both iron doses taken from the 12th to the 36th week of gestation maintained the normal hemoglobin and hematocrit concentrations, but the ferritin concentration in the double-dose group was higher [52]. The second study in Egypt also found no statistically significant difference in the hemoglobin concentrations between a single (27 mg) and a double dose (54 mg) of iron in non-anemic women with twin pregnancy [53]. In both studies, the higher doses, however, led to a higher incidence of the side effects (nausea/vomiting, or noncompliance, constipation, black staining of the stools) [52][53].

What are the iron intake/supplementation recommendations for women pregnant with twins, then, if researchers know from the latest studies that unnecessary iron supplementation may have adverse effects on the course of pregnancy, increasing the risk of pregnancy-induced hypertension, pre-eclampsia and gestational diabetes [39][78].

The latest position statement of the US Preventive Services Task Force is very cautious and indicates there are too little data to estimate the benefits and risks of routine iron supplementation in pregnant women in order to prevent the adverse course of pregnancy and experts from this organization do not take a different stand with regard to multiple pregnancies [79]. The same approach is adopted by the American College of Obstetricians and Gynecologists, and just like the previous opinion, does not refer to iron supplementation in women pregnant with twins [80][81]. Routine iron supplementation for all women is also not recommended in Great Britain. According to British experts, non-anemic women who are at a higher risk of iron deficiency, should be checked for the ferritin concentration already in early pregnancy and, if the concentration is lower than 30 µg/L, dietary supplementation needs to be started. Women with diagnosed iron-deficiency anemia should receive 100–200 mg of elemental iron per day [71]. In Poland, according to the latest recommendations of the Polish Society of Gynecologists and Obstetricians (2020) that take into account the scientific findings about the adverse impact of excessive iron intake, this element should only be taken by anemic women, while in non-anemic women with low

ferritin, dietary supplementation with low iron doses can be recommended from the 16th week of pregnancy (up to 30 mg per day). None of the above guidelines refer specifically to women pregnant with twins [66].

As iron should not be used by pregnant women on their own, its presence in most vitamin-mineral supplements for pregnant women can be problematic. Based on the composition of prenatal supplements commercially available in Poland estimated by Wierzejska in 2019, 82% of them contained iron at doses of 14–60 mg, on average 28.5 mg [82]. At the same time, it is worth mentioning that, recently, the Panel on Dietary Supplements (an advisory body to the Chief Sanitary Inspector in Poland) has established the maximum iron dose in dietary supplements for pregnant women at 30 mg, so that the composition of some preparations will probably have to be changed. According to the Panel's resolution, it is also recommended that such supplements should include the following warning: *"product for pregnant women, use after consulting a doctor"* [83]. However, Ru et al., pose a question in their publication whether the iron content in a standard prenatal supplement commercially available in the USA (27 mg) is sufficient for women with a twin pregnancy [3].

Only experts from North America raise the subject of iron supplementation in women pregnant with twins. The Institute of Medicine in the USA in 1990 considered that women with a multiple pregnancy should take 30 mg of elemental iron per day from the 12th week of gestation [84], while according to the Canadian guidelines, 30 mg of iron is the total daily requirement, of which 27 mg can be supplied by vitamin-mineral supplements and the rest with diet. Higher amounts of iron can only be prescribed by a physician [36]. In the face of the worldwide lack of specific guidelines for women pregnant with twins, a special approach to iron intake with diet and optimal supplementation is certainly required for women with a twin pregnancy who are on a plant-based diet, e.g., vegetarian or vegan.

4.2. Calcium

Apart from iron, another mineral that is particularly important during pregnancy is calcium. However, available studies do not provide a conclusive answer to the question of whether calcium serum concentrations differ between women with a twin pregnancy and women with a singleton pregnancy. In an Indian study, it was demonstrated that the calcium blood concentration in women with a twin pregnancy at birth was statistically significantly lower than in women with a singleton pregnancy (8.7 mg/dL vs. 9.1 mg/dL), which resulted in the same lower calcium concentration in the newborns' cord blood (9.6 mg/dL vs. 9.9 mg/dL) [44]. In a Japanese study, calcium concentrations determined in the 25th and 30th week of pregnancy in women pregnant with twins was higher than in women with a singleton pregnancy, but the difference blurred in the 36th week of pregnancy. At the same time, it was found that bone resorption markers in women pregnant with twins were statistically significantly higher compared to women with a singleton pregnancy [48], which also had been previously observed by Okah et al. [50]. Experts believe that this stems from a physiological mechanism that allows women pregnant with twins to meet the fetal calcium requirements and, at the same time, confirms that this element is extremely important in the maternal diet [48].

According to Canadian Alberta Health Services, a twin pregnancy requires additional amounts of calcium in the diet and the total calcium intake should amount to 2000–2500 mg per day [36]. The Institute of Medicine recommends supplementing 250 mg per day after the 12th week of gestation [84], while Luke argues that 3000 mg of calcium needs to be supplemented [85]. Such a high requirement for this nutrient would mean that the increased calcium absorption during pregnancy, which is caused by the higher concentration of the active metabolite of vitamin D (calcitriol), is not sufficient to cover the needs of both fetuses. At the same time, experts recommend that a single dose of a calcium preparation should not exceed 500 mg in order to ensure the maximum absorption of this element and minimize adverse reactions (flatulence, constipation). It is suggested that calcium should be taken in the form of single preparations and at least 2 h apart from taking a multi-nutrient preparation containing iron because these nutrients interact with each other, causing lower calcium bioavailability [36]. It is believed that calcium supplementation in a twin pregnancy is particularly important in very young women and in women who supply little calcium in their diet [17][37]. According to Luke, calcium supplementation has been proven to reduce the risk of gestational hypertension [77].

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