

REVIEW ARTICLE

Relationship between Vitamin D, Calcium, Protein, Fruits and Vegetables and Bone Health in Children with Type 1 Diabetes Mellitus

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Abstract

Several studies suggest that Type 1 Diabetes Mellitus is associated with changes in bone mineral density (BMD), resulting in the development of bone abnormalities such as osteoporosis and osteopenia. Some nutrients such as vitamins, minerals and macronutrients, and other nutritional components present in fruits and vegetables may play a role in bone metabolism. This non-systematic review aims to examine the relationship between nutritional components such as vitamin D, calcium, proteins, fruits and vegetables in bone health in children and adolescents with diabetes.

Methods: The search was carried out using online databases (Pubmed, Scopus and SciELO), including articles with at least 30 references that have been cited at least one time in Index Medicus, resulting from the keywords "Bone Mineral Density"; "Calcium"; "Protein"; "Vitamin D"; "Fruits and Vegetables"; "Type 1 Diabetes Mellitus"; "Children".

Results: Out of 735 articles initially retrieved, 90 met with the inclusion criteria.

Conclusions: It has been widely reported that nutritional factors could prevent or modify bone mineral content and BMD, more research is necessary to assess the effects of lifestyle interventions, dietary components and recommended dosage for nutrient intake on BMD and turnover in children with type 1 diabetes mellitus.

Keywords

Bone Mineral Density; Calcium; Protein; Vitamin D; Fruits and Vegetables; Type 1 Diabetes Mellitus; Children

Introduction

There is controversy regarding the incidence of risk in bone health in pediatric patients with type 1 diabetes mellitus (T1DM). Concordantly with other studies,^{1,2} we have recently reported no differences in bone mineral density (BMD) between children and adolescents with T1DM and control subjects.³ However, other publications have reported that children and adolescents with T1DM have a greater risk of lower BMD, which could interfere with achieving maximum bone mass and increase the risk of osteoporosis.⁴⁻⁷ Furthermore, it has been reported that longer duration of diabetes in children is associated with shorter and slender



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bones, probably increasing the risk of fractures in the future.⁸ Several mechanisms have been proposed to explain the relationship between T1DM and BMD, including: i) lower circulating insulin-like growth factor-1 (IGF-1) levels, resulting in a decrease in their potential for growth; ii) hyperglycemia as an important factor with adverse effects on the function of osteoblasts and bone formation; iii) insulin deficiency, resulting in loss of bone anabolic action; iv) an altered vitamin D metabolism that may exert immunomodulatory effects; and v) an increased urine calcium excretion that leads to a negative calcium balance.^{9,10} However, most of these mechanisms are not fully understood.

The gold standard for quantitative measurements of bone density and bone mineral content (BMC) is dual-energy X-ray absorptiometry (DEXA) both adults and children, preferred over other techniques because of its speed, precision, safety, low cost, and widespread availability. In the pediatric population, BMD values from DEXA are influenced by puberty, sex and ethnic differences.^{11,12} Clinical biomarkers of bone health, either in serum or urine, primarily correspond to changes in levels of bone formation markers such as alkaline phosphatase, osteocalcin and procollagen I propeptides¹³ and resorption markers like collagen degradation products (hydroxyproline, hydroxylysine and cross-linked telopeptides of type I collagen).^{14,15} In children, there are higher concentrations of bone biomarkers than in adults due to both skeletal growth and rapid bone turnover during childhood and adolescence. These markers can be used as an indicator of bone metabolism and are significantly affected by physiological conditions (age, gender, growth velocity, nutritional status and pubertal status) and pathologies (prematurity, growth hormone deficiency, malnutrition, malabsorption, vitamin D deficiency, and metastatic bone disease).¹⁶

Physical activity and nutrition are some of the main modifiable factors with a strong influence on the accretion and maintenance of bone mass.^{17,18} There is a well-established importance of nutrients such as proteins, potassium, magnesium, zinc, copper, iron, fluorine, vitamin A, D, C, K and from fruits and vegetables (FV) in normal metabolic bone growth.^{19,20} Children with a dietary pattern characterized by high intakes of dairy and cheese, whole grains, and eggs during early infancy, have a higher BMD during childhood.¹² Whereas, a study of 622 twins aged 7–15 from South China showed a negative correlation between fat intake and BMD.²² Indeed, a relationship has been established between maternal dietary pattern during pregnancy and bone mass of children at 9 years of age.^{19,23} Maggio *et al.* showed that patients with T1DM have lower levels of bone biomarkers, which are positively correlated with lower calcium intake.¹ Although several results have been obtained in animal models,^{24,25} the role of a diet in children and adolescents with T1DM has not been fully studied. In this non-systematic review, we examine the evidence of whether nutritional components such as calcium, vitamin D, protein and FV affect the BMD in children and adolescents with T1DM.

Methods

A non-systematic review was conducted to evaluate the relationship between dietary factors and their effect on bone health in children and adolescents with T1DM. The search was carried out using online databases (Pubmed, Scopus and SciELO), including articles with at least 30 references that had been cited at least once in the Index Medicus, as a result of the key words "Bone Mineral Density"; "Calcium"; "Protein"; "Vitamin D"; "Fruits and vegetables"; "Type 1 Diabetes Mellitus"; "Children"; "Adolescents". Other search strategies between bone health and T1DM were: "clinical biomarkers" and "T1DM" or "DEXA" and "T1DM". The studies were filtered automatically and manually by reading the bibliography obtained. The articles were chosen according to the following criteria: Type of Study (experimental studies, clinical studies, randomized and controlled trials, case-control studies), Publication Types (meta-analysis, clinical practice guidelines, review), Subjects of Study: humans (children and adolescents) and animals. After the two-step filter, the process was completed with a cluster search based on the bibliography of the published publications. The initial amount was 735, with final number reduced to 90.

Results

Calcium

Among the pediatric T1DM population, numerous factors may contribute to the development of osteopenia. Children and adolescent with T1DM present chronic calcium deficiency as a result of increased urinary calcium excretion coupled with diminished calcium

absorption.^{5,26} Karaguzel *et al.* found that children with T1DM had lower levels of calcium in serum compared to healthy children. Similarly, in two different studies done in Egyptian adolescents and children with T1DM, significantly lower serum calcium levels were reported when compared to the control group.^{27–29} A reduction in serum calcium levels together with an increased urinary calcium excretion would induce a compensatory increase in parathyroid hormone (PTH) secretion, stimulating bone resorption by osteoclasts.²⁷ Furthermore, both studies showed that serum calcium levels were significantly associated with a decrease of 25-hydroxycholecalciferol (25(OH)D) levels in serum, possibly due to the central role of vitamin D in intestinal calcium absorption and homeostasis. In contrast, several studies have reported that serum calcium levels are maintained within the normal range in T1DM children and adolescents, with no differences compared to healthy pediatric population.^{6,30,31} These discrepancies could be explained by study population differences in sun exposure, calcium intake and, BMI, considering obesity as a predisposing factor of metabolic acidosis and its consequent alteration of bone metabolism.^{32,33}

On the other hand, a positive correlation between BMD and calcium intake in healthy children and adolescents has been reported.³⁴ Cross-sectional studies in Caucasian and Chinese children showed a positive relation between calcium intake and BMD while reports related to calcium intake in the pediatric T1DM population are variable.^{35–38} Although few studies have shown an association between T1DM, calcium intake and BMD, it has been proposed that all children with T1DM should have an adequate daily intake of calcium (1200 mg/day).^{26,29} In accordance with international organizations guidelines (e.g., World Health Organization (WHO), National Academy of Sciences (NAS)) a daily calcium intake higher than 1000 mg should be recommended for healthy children. The Institute of Medicine (IOM) suggests a Recommended Dietary Allowance (RDA) of 1300 mg/day of calcium for children and adolescents 9 years old or older, 700 and 1000 mg/day for children between 1–3 and 4–8 years of age, respectively, and adequate intake (AI) of 200 and 260 mg/day for infants 0 to 6 months and 7 to 12 months old. Recently, new recommendations from the European Society for Pediatric Endocrinology have indicated that levels of dietary calcium intake for children over 12 months of age are considered sufficient over 500 mg/d, insufficient between 300–500 mg/d and deficient when lower than 300 mg/d.⁴⁰ (Table 1).

Table 1. Recommended dietary intake of nutrients and fruits and vegetables for pediatric patients with Type 1 Diabetes Mellitus.

Variables	Source	Daily Recommendation
Calcium	DRIs 2011 ⁴⁵	Infants 0 to 6 months: 200 mg/d Infant 6 to 12 months: 260 mg/d Children 1 to 3 years: 700 mg/d Children 4 to 8 years: 1000 mg/d Males and females 9 to 18 years: 1300 mg/d
Vitamin D	DRIs 2011 ⁴⁵	Infants 0 to 12 months: 400 UI/d Children and Adolescents: 600 UI/d
Proteins	ISPAD 2014 ⁷⁰	Protein 15% to 20% of total energy intake
Fruits and Vegetables	Yngve <i>et al.</i> 2005 ⁸⁵	FV ≥ 400 g/day or Fruit: 1 to 5 portions/day and Vegetable: 2 to 5 portions/day

DRIs: dietary reference intakes; FV: fruits and vegetables; ISPAD: International Society for Pediatric and Adolescent Diabetes

Vitamin D

In humans, vitamin D3 (cholecalciferol) is synthesized in the skin by ultraviolet B radiation from sunlight (230–313 nm), which stimulates 7-dehydrocholesterol in the keratinocytes, being the main source for vitamin D.³² Additionally, the dietary form of Ergocalciferol (vitamin D2) was provided by our diet. The main sources are cod liver oil, oily fish (e.g., salmon, mackerel, sardines, tuna fish), vitamin D-fortified milk and other fortified foods. Both, vitamin D2 and vitamin D3 can be hydroxylated in the liver to 25-hydroxycholecalciferol [25(OH)D], which is finally converted in the kidney to the biologically active metabolite 1,25-dihydroxycholecalciferol [1,25(OH)2D], also called calcitriol. Calcitriol is a steroid hormone known for its role in calcium and bone metabolism and is newly recognized as a potent modulator of proliferation, cell differentiation and immune response in many tissues.^{32,41}

Despite the fact that serum 25(OH)D levels are the best indicator of vitamin D status, the concentration that constitutes vitamin D deficiency is still controversial.⁴² The American Academy of Pediatrics (AAP) and the IOM have defined vitamin D insufficiency as serum 25(OH)D levels below 20 ng/mL;⁴² whereas the Endocrine Society has established a cut-off of serum insufficiency of 25(OH)D levels below 30 ng/mL,^{29,33,42,43} while vitamin D toxicity is defined as hypercalcemia and serum 25(OH)D upper 250 nmol/L, with hypercalciuria and suppressed PTH. Intoxication is predominantly seen in infants and young children after exposure to high doses of vitamin D (240,000 to 4,500,000 IU).⁴⁰

Currently, the AAP and IOM recommend 400 UI/day of vitamin D for children aged less than 1 year and 600 UI for children aged 1 year or more.^{40,43,44,45} Both guidelines are for healthy infants, children and adolescents. Furthermore, special considerations must be taken into account in different clinical situations and other conditions as seasonality, sun exposure and use of sunscreen, food fortification, races among others.^{32,33,42,46}

The role of vitamin D in the development of T1DM remains controversial. It has been recognized that vitamin D deficiency increases the risk of developing T1DM as well as type 2 diabetes mellitus (T2DM).^{47,48} A meta-analysis suggested that the risk of T1DM was significantly reduced in those children who were supplemented with vitamin D during childhood compared to those who were not.⁴⁹ Daga *et al.* reported that serum 25(OH)D levels were significantly lower in patients with T1DM and T2DM under 25 years (with an average age of 16.7) compared with control subjects. Specifically, serum 25(OH)D levels were slightly lower in the group with T1DM compared with T2DM patients.⁵⁰ Along with this, a high prevalence of vitamin D deficiency has been observed in a prospective cross-sectional study in children and adolescents with T1DM, where 60.5% presented 25(OH)D levels under 20 ng/mL.³³ In contrast, recently Mäkinen *et al.* conducted of 3702 prospective serum samples from 252 children for 25(OH)D from the age of 3 months onward until diagnosis of T1DM. At the end, there are no apparent differences in the circulating 25(OH)D concentrations between children who progressed to T1DM and children who remained unaffected.⁵¹ A case-control study in children and adolescents with T1DM and controls from Australia (latitude 27.5°S) reported lower serum 25(OH)D in a control group than in T1DM patients.⁵² Similar results were observed in another study in children and adolescents with T1DM compared with controls.²⁷ These contradictory results could be due to differences in geographic areas which is directly associated to exposure to ultraviolet radiation and the influence of markers of adiposity such as BMI in adults and children; HDL-cholesterol levels and programs for food fortification with vitamin D.^{53–57} On the other hand, it is possible that low 25(OH)D concentrations appear after diagnosis because the disease can affect the metabolism of vitamin D and associated complications such as loss of the vitamin D-binding protein via excretion into urine.⁵⁸ Multiple studies have assessed the relationship between vitamin D and BMD in pediatric population with T1DM. A study in T1DM patients aged 3 to 15 years showed that mean serum 25(OH)D levels were significantly lower when compared to control groups. In addition, 94.74% of T1DM children had an abnormal bone state (i.e., osteoporosis and osteopenia) in their arms and 100% of them had insufficient levels of vitamin D (<20 ng/mL) and an abnormal bone state in ribs. This difference was significantly different when compared with patients with sufficient serum 25(OH)D (≥21 ng/mL) levels.²⁸ Similarly, a cohort of children with T1DM in Slovakia found similar results, where nearly two-thirds of children had insufficient vitamin D levels and had significantly lower Z scores of the lumbar spine compared with children with sufficient vitamin D levels.⁵⁹ In addition, a prospective study, done in pre-pubertal and adolescents girls aged 9 to 15 years, reported that basal concentrations of serum 25(OH)D levels were

associated with changes in BMD in the lumbar spine and femoral neck. Girls with serum 25(OH)D levels under 37.5 nmol/L had a 4% lower increment of BMD from the onset of the study.⁶⁰ In contrast, in a previous study by our team, we reported a normal BMD in T1DM children, where more than 95% of them had insufficient or deficient vitamin D levels.³ Other studies in adolescent and adults with T1DM did not find differences in serum 25(OH)D levels between T1DM patients with a control group, neither association between serum 25(OH)D levels and BMD for total body and lumbar spine.³⁷ Meanwhile, a study of 100 Turkish children and adolescents (aged between 4.7 and 19.9 years) with T1DM found no differences in 25(OH)D levels between groups with normal BMD (Z-score ≥ -1), low BMD (Z-score ≤ -2) and BMD in the low-normal range (Z-score -2 to -1), even though 28% and 43% of patients presented vitamin D deficiency and insufficiency, respectively.⁶¹ Furthermore, a study of 27 subjects with recent-onset T1DM (age at diagnosis of 10 to 35 years) showed that markers of bone formation and bone resorption did not change significantly at 1-year of follow-up.⁶²

Studies in animal models have tried to answer the role of vitamin D on the bone repair process in the presence of diabetes. Mao *et al.* showed that vitamin D deficiency aggravated the decrease in BMD in diabetic female mice induced by streptozotocin.⁶³ In parallel, administration of 250 mg of calcitriol to an experimental model of diabetes in rats, drastically decreases the percentage of diabetes in animals along with an increase BMD, reaching similar values as the control group.⁶⁴ Although the association between BMD and serum 25(OH) D concentration is weak, the bioavailable vitamin D (as the fraction that is both free and albumin bound) has been closely associated with BMD (spine, neck and hip).⁴⁶

Given the negative effects of vitamin D deficiency and T1DM on bone health, patients with both conditions have multiple risk factors for increased skeletal fragility.²⁹ Although no specific recommendations for patients with T1DM have been proposed, higher intakes of vitamin D has been suggested to prevent the disease with a duration of therapy appropriate for a minimum of 12 weeks considering recommendations for the treatment of nutritional risks.^{40,44}

Proteins

Protein intake is essential for bone health because the consumption of calcium and protein-rich foods during infancy and adolescence are important for obtaining the maximum bone mass.^{21,65} In children and adolescents, the current RDA for Boys and Girls, 1–3 years, 1.05 g/kg/d or 13 g/d of protein, 4–8 years, 0.95 g/kg/d or 19 g/d of protein, 9–13 years, 0.95 g/kg/d of 34 g/d of protein and RDA for Boys 14–18 years, 0.85 g/kg/d of protein or 52 g/d of protein RDA for Girls 14–18 years, 0.85 g/kg/d of protein or 46 g/d of protein.

Protein intake has been proposed as one of the mechanism associated with BMD. However, the relationship between protein intake and bone health is controversial, as it has been observed that protein intake increases urinary calcium, resulting in greater bone resorption.⁶⁵ In a review by Mangano *et al.* two meta-analyses in adults concluded that protein intake is not negative for bone health and may be influencing positively the BMD. In accordance with this, a recent review of 2018 in adults concluded “higher protein intakes, whatever their origin (animal or vegetable), do not appear to contribute to the development of osteoporosis or to increase fracture risk.”⁶⁶ With intakes above the current RDA, dietary protein is rather beneficial in reducing bone loss and fracture risk, especially at the hip, provided calcium intakes are adequate. Insufficient dietary protein intakes may be a much more severe problem than protein excess”.⁶⁷

On the other hand, in children, Bounds *et al.* reported that protein intake is positively related to BMD at the age of 8 years.⁶⁸ In accordance with this, a prospective study in healthy children and adolescents between 6 and 18 years showed a positive association between protein intake and the improvement of bone variables, such as bone cortical areas and bone mineral content after adjusting for age, sex, body mass index (BMI), growth rate and pubertal development.⁶⁹ Furthermore, an inverse association was found between the net acid load of the diet and the cortical area and bone mineral content. In the long term, a high protein intake is associated with the bone variables as an anabolic factor, whereas diets with a high acid load are associated with those variables as a catabolic factor.⁷⁰

One of the proposed mechanisms is that protein induced-anabolic action is mediated through an increase of IGF-1.^{65,66} Circulating IGF-1 produced by the liver, is structurally similar to insulin.³⁷ A positive association between protein intake and IGF-1 concentrations in healthy children has been reported.⁷¹ In a similar result, Esterle *et al.* found in their study of 192 healthy

adolescent girls, that milk consumption was positively associated with BMD and serum IGF-1.⁷²

In terms of the catabolic effect, high-protein diets are proposed to increase bone resorption through the oxidation of the sulphur contents in two amino acids (methionine and cysteine) to sulphuric acid, with a resulting reduction in blood pH. However, the catabolic effect is also influenced by the alkaline load of the diet (potassium, calcium and magnesium), which neutralizes pH.⁶⁵ The results of a study by Alexy *et al.* and a recent review by Jesudason *et al.* indicate that it is necessary to achieve a protein-rich diet combined with high FV intake.^{65,69}

Although there is little evidence of the relationship of proteins in bone health in diabetic children, in the latest update from International Society for Pediatric and Adolescent Diabetes (ISPAD),⁷³ there are specific recommendations for protein intake for children and adolescents with T1DM, given as a percentage of daily total energy intake from proteins: 15% to 20%.

In recent studies of dietary intake in children and adolescents with T1DM, results showed that the percentage of energy intake from protein ranged from 15.7% to 21.4% (Table 2).

Fruits and Vegetables

In 1968 Wachman and Bernstein suggested that diet is related to the development of osteoporosis through the regulation of acid-base balance.⁶⁵ The diet included foods that contributed to the acid load (e.g., those rich in proteins, grains and cereals) as well as foods that provide alkaline products for neutralizing the acid load (e.g., FV). Nowadays, diet is characterized by a low consumption of FV and high protein intake. FV are rich sources of bases such as calcium, citrate, magnesium and potassium, which act as buffers against the acid load and maintain the plasma pH within the normal limits in this type of diet. Several authors have reported that low intake of FV leads to a decline of BMD,^{74,75} however the literature is still contradictory. In a recent prospective, multiethnic, population-based cohort study of 2850 children, no association was found between dietary acid load during early life and bone health during childhood measured through DEXA.⁷⁶ Potassium is one of the nutrients present in higher levels in FV, which may have an effect on bone health. This effect could be due to its role as a buffer in the acid-base balance, and also by an association with decreased urinary calcium (when administered as potassium citrate or bicarbonate salts or from FV). However, more studies are needed to confirm these potential mechanisms.⁷⁷

The study by Tylavsky *et al.* is a clear example of relating FV intake to bone mass.⁷⁴ This study evaluated the influence of FV intake on the excretion of urinary calcium and bone mass by DEXA in 56 healthy girls aged 8 to 13 years. After adjusting for age, BMI, and physical activity, the study showed that girls eating three or more servings of FV each day presented greater total body and radial bone mass, lower urinary excretion of calcium and lower PTH levels compared with the girls consuming less than three servings each day. The authors concluded that intake of FV had a beneficial effect on bone mass and that lower excretion of urinary calcium was associated with a high intake of FV. In agreement with these results, McGartland *et al.* evaluated whether intake of FV, as reported by 1345 adolescent boys and girls, aged 12 or 15 years, had influence in BMD was measured by DEXA.⁷⁸ Using multiple linear regression and adjusting for physical activity and lifestyle factors, it was shown that girls in the 12-year-old group that ate high amounts (>196.71 g/day) of fruits had a significantly higher BMD of the heel than those that ate moderate amounts of fruits (83.38 to 196.71 g/day). The authors concluded that fruits, with their alkaline properties, mediated the acid-base balance of the diet. The above results agreed with a longitudinal study that showed that calcium and FV intake, in addition to physical activity, were independent factors for total body bone mineral content in boys from age 8 to 20 years, but not in girls. Girls reported a low intake of FV and calcium, which may explain why this effect was not apparent in them.⁷⁹

Table 2. Review of studies of protein, calcium, vitamin D and fruit and vegetable intake in children with type 1 diabetes mellitus

Author		Country	Subjects (n); age (years)	Protein *	Calcium	Vitamin D	Fruit and Vegetables
Mayer-Davis ⁽⁸⁶⁾	2006	EEUU	1510; 10 – 22 years	15.7%	1251 mg/day	-	Fruits: 1.3 serving/ day Vegetables: 1.7 serving/day
Lodefalk ⁽⁸⁴⁾	2006	Sweden	174; 13-19 years	16%	-	-	Vegetables: 47% daily or more often. Fruit and fruit juice: 68% daily or more often.
Overby ⁽⁸⁸⁾	2007	Norway	177; 9 – 13 years	16.1% – 16.3%	906 mg/day	244 IU	210 g/day
Overby ⁽⁸¹⁾	2007	Norway	550; 2 – 19 years	16.2%	-	-	Fruits: 65.2 g/day Vegetable: 51.5 g/day FVJ: 218 g/day
Papadaki ⁽⁸³⁾	2008	Greece	41; 6 – 17	17%	7% ≤60% RDA 54% ≥ 100% RDA	-	Fruits: 214 ± 150 g/day Vegetables: 196 ± 123 g/day
Galli-Tsinopoulou ⁽⁸⁹⁾	2009	Greece	24; 4 – 16 years	17% 2.06 g/kg/d	93% as a percentage of the DRI	63% as a percentage of the DRI	-
Maggio ⁽¹⁾	2010	Switzerland	27; 10.5 years	41.8 g/day 1.29 g/kg/d	524.1 ± 84.5 mg/d	-	-
Nansel ⁽⁸⁰⁾	2012	EEUU	252; 8 – 18 years	16.1%	-	-	Fruit (not including juice): 1.0 ± 1.1 servings/day Vegetables (not including potatoes): 1.4 ± 1.2 servings/day
Maffeis ⁽⁹⁰⁾	2012	Italy	114; 6 – 16 years	14.7% 62.1 g/d 1.6 g/kg/d	-	-	Fruits/vegetables 20% of prepubertal children had ≥ 5 servings/day; 35.6% of pubertal children had ≥ 5 servings/day.
Mosso ⁽⁸²⁾	2015	Chile	30; 9 – 22 years	118 ± 27.9 g/day 2.6 ± 1.3 g/kg BW 21.4% ± 3.2%	1339.6 mg/d	235.7ug/d	Fruits and vegetables: 3 servings/day

FVJ: Total intake of fruits, vegetables, potatoes and fruit juice. * Percentage (%) of total energy intake

Several studies have evaluated the intake of FV in children and adolescents with T1DM, with controversial results (Table 2). In a recent study by Nansel *et al.* in US children, a low consumption of FV (fruits, 1.0 ± 1.1 servings/day and vegetables, 1.4 ± 1.2 servings/day) was reported; similar results were found in Norwegian adolescents in 2007 (fruit, range from 51 to 82 g/day; vegetables, range from 43 to 67 g/day).^{80,81} Our study of Chilean children and adolescents with T1DM reported consumption of three servings of FV per day.⁸² In contrast, Papadaki *et al.* reported for Greek children an average intake of 214 ± 150 g/day for fruits and 196 ± 123 g/day for vegetables.⁸³ In the latest update of the ISPAD in 2014, there are no

specific recommendations for the consumption of FV in children and adolescents with T1DM.⁷³ The WHO proposed at least 400 g or 5 servings of FV per day for all populations.⁸⁴ Several countries have published the desirable level of consumption of FV for healthy children, with an average of FV ≥ 400 g/day (fruit, 1 to 5 servings per day and vegetables, 2 to 5 servings per day) (Table 1).⁸⁵ One reason for this discrepancy might be due to different eating habits in populations as the European have the Mediterranean diet, which is rich in FV.

In this review, we have suggested that due to harmful effects of T1DM on bone formation and maintenance, special attention should be paid to adequate intake of calcium, vitamin D and protein as well as promoting the intake of FV among children and adolescents with T1DM. To achieve this, we propose the recommendations shown in Table 1.

Conclusions

The relationship between T1DM and BMD has been researched and although several mechanisms have been proposed regarding changes in BMD in patients with T1DM, such as hyperglycemia, hypercalciuria (frequently in the early stages of diabetes), decreased insulin and IGF-1, it is important to highlight that the evidence remains controversial probably due to the difference in the study designs, measurements locations, disease duration and patient selection (age, gender, etc.). Despite this, it has been widely reported that nutritional factors could prevent or modify bone mineral content and BMD as evaluated through newer technologies, such as DEXA. Replacement of vitamin D along with calcium, ideally through the diet, has been found to improve BMD in children with T1DM and prevent osteoporosis; however, the data is not consistent among studies.

Several authors have reported the effects of foods such as milk, other dairy products and FV on bone growth, in children and adolescents. The last review suggested the need to achieve a combination of protein-rich diet with high consumption of FV. In parallel, the ISPAD 2014 recommended the intake of many fresh FV because these are naturally rich in antioxidants (e.g., tocopherols, carotenoids, vitamin C and flavonoids) and are strongly recommended for cardiovascular protection of young people with T1DM. However, more research is necessary to assess the effects of lifestyle interventions, dietary components and recommended dosage for nutrient intake on BMD and turnover among children and adolescent with T1DM with the purpose of improving bone health and preventing fractures.

Conflicts of Interest

The authors have no conflicts of interest to disclose.

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Abbreviations

T1DM: type 1 diabetes mellitus; BMD: bone mineral density; BMC: bone mineral content; DEXA: dual-energy X-ray absorptiometry; IGF-1: insulin-like growth factor-1; FV: fruits and vegetables; PTH: parathyroid hormone; 25(OH) D: 25-hydroxycholecalciferol; BMI: body mass index; WHO: World Health Organization; NAS: National Academy of Sciences; IOM: Institute of Medicine; RDA: Recommended Dietary Allowance; 1,25(OH)₂D: 1,25-dihydroxycholecalciferol; AAP: American Academy of Pediatrics; T2DM: type 2 diabetes mellitus; STZ: streptozotocin; GH: growth hormone; ISPAD: International Society for Pediatric and Adolescent Diabetes

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