High prevalence of iodine deficiency among vegan compared to vegetarian and omnivore children in the Czech Republic: cross sectional study

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Abstract

Background: Vegetarian (VG) and vegan (VN) diets are becoming increasingly popular among children. These restrictive types of diet remain a concern as they may impair growth and development, although up-to-date epidemiological studies are lacking. Iodine, an essential micronutrient, is of specific concern due to its important role in thyroid gland physiology.

Methods: We collected clinical, anthropometric, and blood/urine parameters of iodine status as well as thyroid function among children following VG (n = 91), VN (n = 75), and omnivores (OM, n = 52), aged 5.4 (± 4.3) years.

Results: We found no significant differences in levels of thyroid-stimulating hormone (TSH), triiodothyronine (fT3), or thyroglobulin (TG) between the groups. Thyroxine (fT4) levels were higher in OM compared to VN (15.00 ± 1.73 vs. 16.17 ± 1.82 pmol/L, p < 0.001). There were strong differences in anti-thyroglobulin antibodies (AhTGc) between groups (OM: 2.54 ± 8.31 vs. VG: 16.24 ± 44.46 vs. VN: 13.93 ± 9.16 UI/L, p < 0.001). Iodine concentration in spot urine (UIC) was highest in OM (195.31 ± 105.28 vs VG: 177.27 ± 155.13 vs. VN: 162.94 ± 163.39 µg/L, p < 0.001). The lowest (5.99 µg/L) but also the highest (991.80 µg/L) levels were measured in VN. 31 VN and 31 VG children met the criteria for iodine deficiency (i.e., UIC < 100 µg/L). Children with regular iodine supplementation had higher UIC (p < 0.001).

Conclusion: We observed a higher prevalence of iodine deficiency in VN and VG group than in OM, with possible impact on thyroidal health (i.e., positivity of antibodies). Further research and new guidelines for iodine supplementation among VG and VN children are therefore warranted.

Introduction

Perceived health benefits as well as environmental and ethical reasons are among the causes of the increasing popularity of so called plant-based diets over the past decades (1, 2). The plant-based diets include several patterns with variable restrictions: Vegetarian diets (VG) that can be divided into lacto-ovo-vegetarian (excluding meat and fish), ovo-vegetarian (excluding meat, fish and dairy), lactovegetarian (excluding meat, fish and eggs), and vegan or strict vegetarian diets (VN), the latter excluding all products of animal source (3). The reduction of animal foods has been proposed to negatively affect the long-term safety of these diets (1). Despite online information sources, dietary guidelines on iodine intake among children following vegetarian and vegan diets are inadequate, also considering the growing number of vegetarian and vegan families (4).

Iodine is a micronutrient that is distributed unevenly in our environment, with insufficient soil contents in many areas of the world increasing the risk of low iodine intake. The main sources are iodized kitchen salt, eggs, dairy and seafood (5). Even nowadays the prevalence of iodine deficiency in European countries is 53.8% for adults and 6.3% for children (6). Currently there is no available data on iodine status in the paediatric population consuming plant-based diets. Data among adults shows that excluding all animal sources of iodine from the diet reduces the daily intake of iodine to 30µg, compared to 110–130µg in children who eat a conventional diet including dairy, fish, and meat (7, 8). The prevalence of iodine deficiency among adult vegans living in Europe is higher than in omnivores (9). Long lasting insufficient intake may lead to iodine deficiency disorders (IDD’s). In pregnant women, iodine deficiency may lead to a disruption in the development of the foetal nervous system (10, 11). The most serious form of iodine deficiency is the so-called endemic cretinism (10). A mild iodine deficiency may result in developing endemic cognitive deficits, preventing children from reaching their full cognitive potential (10, 11). In children with severe iodine deficiency a significant decrease in IQ and higher prevalence of goitre have been observed (10, 11). On the other hand, long-term consumption of iodine that exceeds the upper limit of the daily requirement could lead to thyroid disease, as well (12, 13). To this end we aimed to examine the nutritional intake and biomarkers of iodine status in children following vegan and vegetarian diets and to compare them with values of children regularly consuming animal foods.

Materials And Methods
Study Design and Participants

Two hundred and twenty-two children (n = 92 VG, n = 78 VN, and n = 52 OM controls) were recruited for the study through a network of general practitioners, social media and vegan-focused web pages between November 2019 and July 2021. The inclusion criteria for participants were (1) self/parent-reported vegetarian or vegan or omnivorous children (“Omnivore” (OM) if eating meat, dairy, and eggs on a regular basis, as “Vegetarian” (VG) if not eating meat/meat products/fish, but consuming dairy/eggs, and as “Vegan” (VN) if not consuming any food of animal origin), (2) age of 0–18 years. Subjects with any chronic disease, namely diseases that could affect nutrient absorption (e.g., enteropathy, pancreatic insufficiency, metabolic diseases such as phenylketonuria, or fructose malabsorption criteria) were not enrolled. All procedures took place at the Department of Paediatrics, Third Faculty of Medicine, Charles University, University Hospital Královské Vinohrady (Fig. 1).

The study was conducted according to the Declaration of Helsinki guidelines and approved by the Ethics Committee of the Third faculty, Charles University, Prague, and Ethics Committee of Faculty Hospital Královské Vinohrady. All examinations were performed with parental written consent, with no financial incentives.

Examination, medical history

Structured medical interviews performed by trained clinicians were conducted. Examinations were focused on dietary habits (self-identification as VN/ VG/ OM) and iodine intake. Specifically, the use of iodine supplements and their dosages (in μg), frequency of usage (e.g., daily, twice, or three times a week), and regularity (e.g., regular, irregular) were assessed by questionnaires.

Laboratory analysis

Blood was obtained from a venepuncture after an overnight fast. Urine was also collected after an overnight fast as spot urine morning sample. In some cases, i.e., among nurslings and infants the blood samples and urine samples were obtained only after a breastfeeding or a small breakfast. Biomarkers of interest were serum Thyroid-stimulating hormone (TSH), free thyroxine (fT4), free Triiodothyronine (fT3), Thyroglobulin (TG), spot urine iodine (UIC) and levels of antibodies, i.e., Anti-thyroid Peroxidase Antibody (aTPO) and Antithyroglobulin antibody (AhTGc) were measured. The serum analyses were performed immediately after blood draw in the ISO-certified institutional laboratory by validated routine methods. All three parameters TSH, fT4 and fT3 were analysed by chemiluminescence immunoassay automatically on the Siemens Atellica Solution system. For TG measurements, the electrochemiluminiscent elecsys TG assay on the Roche Cobas e411 analyser was used. UI was assessed using high performance liquid chromatography. For all parameters we used reference values provided by the manufacturer (Table 1).
Table 1
Reference intervals of the laboratory parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>6 months–2 years</th>
<th>2 years–12 years</th>
<th>12 years–18 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Thyroid-stimulating hormone (TSH)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower Reference Limit</td>
<td>0.87 (mUI/L)</td>
<td>0.67 (mUI/L)</td>
<td>0.48 (mUI/L)</td>
</tr>
<tr>
<td>Upper Reference Limit</td>
<td>6.15 (mUI/L)</td>
<td>4.16 (mUI/L)</td>
<td>4.17 (mUI/L)</td>
</tr>
<tr>
<td><strong>Thyroxine (fT4)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower Reference Limit</td>
<td>12.1 (pmol/L)</td>
<td>11.1 (pmol/L)</td>
<td>10.7 (pmol/L)</td>
</tr>
<tr>
<td>Upper Reference Limit</td>
<td>18.6 (pmol/L)</td>
<td>18.1 (pmol/L)</td>
<td>18.4 (pmol/L)</td>
</tr>
<tr>
<td><strong>Triiodothyronine (fT3)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower Reference Limit</td>
<td>5.1 (pmol/L)</td>
<td>5.1 (pmol/L)</td>
<td>4.7 (pmol/L)</td>
</tr>
<tr>
<td>Upper Reference Limit</td>
<td>8.0 (pmol/L)</td>
<td>7.4 (pmol/L)</td>
<td>7.2 (pmol/L)</td>
</tr>
<tr>
<td><strong>Thyroglobulin (TG)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower Reference Limit</td>
<td>3.5 (µg/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper Reference Limit</td>
<td>77.0 (µg/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Iodine in spot urine (UI)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower Reference Limit</td>
<td>&gt; 100 (µg/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild iodopenia</td>
<td>50 (µg/L)</td>
<td>100 (µg/L)</td>
<td></td>
</tr>
<tr>
<td>Moderate iodopenia</td>
<td>20 (µg/L)</td>
<td>50 (µg/L)</td>
<td></td>
</tr>
<tr>
<td>Severe iodopenia</td>
<td>0 (µg/L)</td>
<td>20 (µg/L)</td>
<td></td>
</tr>
</tbody>
</table>

TSH, fT4, fT3 analysed by chemiluminescence immunoassay automatically on the Siemens Atellica Solution system. TG by electrochemiluminiscent elecsys TG assay on the Roche Cobas e411 analyser. UI by liquid chromatography. Reference values provided by the manufacturer.

Nutritional assessment

We used 3-day weighted dietary records to assess iodine intake in our VG, VN and OM participants. Parents weighed and recorded all beverages and food consumed by their children over three days (weekends and weekdays) using electronic kitchen scales. The start of the dietary record was chosen by the parents of the participating children and the record was conducted for a given period of three consecutive days. When exact weighing was not possible—e.g., in case of eating out — household measures (e.g., spoons, cups, slices) and a photo booklet with food in child portion sizes, supplemented with special VG and VN food, allowed semiquantitative recording. An assessment of missing data was done by the study staff, who requested missing information from the parents via electronic communication. Breast milk intake was estimated from maternal registrations and general recommendations for breast milk intake. Food sources of iodine were manually selected from all collected 3-day dietary records. Nutrient data, especially iodine content of the foods was subsequently searched in the Czech database NutriDatabaze.cz, version 8.2, ÚZEI, Praha (http://www.nutridatabaze.cz/), which is part of EuroFIR (https://www.euror.org/food-information/food-composition-databases/). If a food that is a source of iodine did not have its iodine content listed in the Czech database, the food was searched in the USDA, FDA, and ODS-NIH database for iodine content in common foods Release 2.0 (2022; https://www.ars.usda.gov/northeast-area/beltsville-md-bhnrc/beltsville-human-nutrition-research-center/methods-and-application-of-food-composition-laboratory/mafcl-site-pages/iodine/). For products which were used exclusively in Europe (e.g., infant formula) but not listed in NutriDatabase.cz, the dietitian based the iodine content on the product packaging. Iodine-containing supplements were not considered for this analysis of iodine intake. All
basic calculations (iodine amount based on the amount of food consumed) were performed by a dietitian in EXCEL OFFICE and the iodine intake for all 3 days was averaged (Table 2).

Table 2

<table>
<thead>
<tr>
<th>Age group</th>
<th>RDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children 0–59 months</td>
<td>90</td>
</tr>
<tr>
<td>Children 6–12 years</td>
<td>120</td>
</tr>
<tr>
<td>Adolescents</td>
<td>150</td>
</tr>
<tr>
<td>Pregnant and lactating women</td>
<td>250</td>
</tr>
</tbody>
</table>

Anthropometrics

Body height and body weight were measured as the average of three independent measurements using calibrated scales. Infantometer was used to measure the length of nurslings and toddlers, older children's heights were measured by stadiometer. The values were transformed to percentiles using standard percentile graphs validated for use in the Czech Republic (publicly accessible online: “6. National Anthropological Research 2001”) (14).

Statistical analysis

Participants were divided into three self-reported dietary groups (VG, VN and OM). For VG and VN, participants were further classified according to their supplementation habits as supplementing or not supplementing. Participants were further classified based on the fulfilment of the laboratory criteria for iodine deficiency based on different markers. For descriptive analyses, mean and standard deviations were calculated for continuous variables. Moreover, minimum, and maximum values captured are reported. Categorical variables are reported as the proportion of participants in every category. To describe the association of the diets with iodine status, differences between dietary and supplementation groups were calculated for continuous variables as effect size with corresponding 95% confidence intervals and p-values using Wilcoxon signed-rank tests. Moreover, linear regression model was calculated for the relation between log-transformed continuous values and type of diet, with adjustment for age and sex. For categorical variables, the chi-square test was used to calculate p-values for differences between groups. The statistical analysis was done using RStudio software.

Results

3.1. Sample Characteristics

The final sample consisted of n = 222 children, i.e., n = 92 VG, n = 78 VN and n = 52 OM. The mean age of participants was 5.4 years (± 4.3 years) for VG, 4.4 years (± 5.5 years) for VN and 6.7 years (± 5.6 years) for OM and ranged from 0.5 to 18.5 years overall. The median age was 4.0 years for VG, 2.0 years for VN and 4.5 years for OM. There were no significant differences in sex, height percentile, weight percentile, or BMI percentile across the groups, but we observed a higher number n = 7 of VN children with lower BMI i.e., below the 3rd percentile (p = 0.006).

3.2. Iodine Dietary and Supplement Intake Analysis
According to our data a 100% (n = 52) of OM children did not take any supplements with iodine content, following by 83.7% (n = 77) VG and 78.2% (n = 61) VN children. There was a significant difference with moderate effect size in mean intake of iodine (without supplements) between OM (56.58 µg/day ± 38.34), with the highest intake and VN (33.86 µg/day ± 39.78) group with the lowest intake (p < 0.001). We also observed a significant difference in supplement use between VN (26.54 µg/day ± 55.95) / VG (16.83 µg/day ± 41.82) group and OM (0.00 ± 0.00) (p < 0.001). The supplement use was assessed after parents filled questionnaires under medical supervision. A participant who did not take any supplements containing iodine, they were classified as "No" in supplement use. On the other hand, use of supplements classify as “Yes”. The dietary intake was calculated as an average from the reported 3 days (Table 3) and (Fig. 2).
### Table 3
Cross-sectional comparison of Iodine intake and Selected blood markers between omnivore, vegetarian and vegan children aged 0–18 years

<table>
<thead>
<tr>
<th>Iodine intake</th>
<th>Control OM (n)</th>
<th>Min</th>
<th>Max</th>
<th>Mean (± SD)</th>
<th>Diet (n)</th>
<th>Min</th>
<th>Max</th>
<th>Mean (± SD)</th>
<th>p*</th>
<th>Adj.p**</th>
<th>Effect size CI 95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDI</td>
<td>42</td>
<td>0.40</td>
<td>202.10</td>
<td>56.58 (±38.34)</td>
<td>VG (89)</td>
<td>0.00</td>
<td>625.50</td>
<td>59.59 (±82.18)</td>
<td>0.24</td>
<td>0.49</td>
<td>0.26 (0.18–0.33)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>VN (72)</td>
<td>0.00</td>
<td>210.00</td>
<td>33.86 (±39.77)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>0.31 (0.23–0.40)</td>
</tr>
<tr>
<td>Dose</td>
<td>52</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00 (±0.00)</td>
<td>VG (92)</td>
<td>0.00</td>
<td>200.00</td>
<td>16.83 (±41.82)</td>
<td>&lt; 0.001</td>
<td>0.005</td>
<td>0.10 (0.13–0.46)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>VN (78)</td>
<td>0.00</td>
<td>200.00</td>
<td>26.54 (±55.95)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>0.31 (0.23–0.40)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Blood markers of iodine status</th>
<th>Control OM (n)</th>
<th>Min</th>
<th>Max</th>
<th>Mean (± SD)</th>
<th>Diet (n)</th>
<th>Min</th>
<th>Max</th>
<th>Mean (± SD)</th>
<th>p*</th>
<th>Adj.p**</th>
<th>Effect size CI 95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH [mUI/L]</td>
<td>52</td>
<td>0.77</td>
<td>6.70</td>
<td>2.59 (±1.42)</td>
<td>VG (91)</td>
<td>0.84</td>
<td>7.87</td>
<td>2.53 (±1.15)</td>
<td>0.75</td>
<td>0.79</td>
<td>0.03 (0.00–0.21)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>VN (75)</td>
<td>0.67</td>
<td>11.69</td>
<td>2.62 (±1.66)</td>
<td>0.90</td>
<td>0.91</td>
<td>0.01 (0.00–0.20)</td>
</tr>
<tr>
<td>fT4 [pmol/L]</td>
<td>52</td>
<td>11.21</td>
<td>18.16</td>
<td>15.00 (±1.73)</td>
<td>VG (91)</td>
<td>11.23</td>
<td>21.75</td>
<td>15.58 (±2.16)</td>
<td>0.18</td>
<td>0.01</td>
<td>0.11 (0.01–0.26)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>VN (75)</td>
<td>11.69</td>
<td>21.94</td>
<td>16.17 (±1.82)</td>
<td>0.00</td>
<td>0.21</td>
<td>0.28 (0.11–0.44)</td>
</tr>
<tr>
<td>fT3 [pmol/L]</td>
<td>52</td>
<td>4.92</td>
<td>8.53</td>
<td>6.96 (±0.78)</td>
<td>VG (91)</td>
<td>4.09</td>
<td>16.16</td>
<td>7.22 (±1.32)</td>
<td>0.26</td>
<td>0.52</td>
<td>0.09 (0.00–0.26)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>VN (74)</td>
<td>3.42</td>
<td>9.49</td>
<td>7.15 (±1.01)</td>
<td>0.09</td>
<td>0.77</td>
<td>0.15 (0.01–0.33)</td>
</tr>
<tr>
<td>UIC [µg/L]</td>
<td>52</td>
<td>40.80</td>
<td>494</td>
<td>195.31 (±105.28)</td>
<td>VG (90)</td>
<td>15.70</td>
<td>787.00</td>
<td>177.27 (±155.13)</td>
<td>0.03</td>
<td>0.01</td>
<td>0.18 (0.03–0.33)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>VN (75)</td>
<td>5.99</td>
<td>991.80</td>
<td>162.94 (±163.39)</td>
<td>0.01</td>
<td>0.12</td>
<td>0.25 (0.09–0.42)</td>
</tr>
</tbody>
</table>

TSH = Thyroid-stimulating hormone, fT4 = free thyroxine, fT3 = free Triiodothyronine, TG = Thyroglobulin, UIC = spot urine iodine, OM = omnivore, VG = vegetarian, VN = vegan, n = number of subjects, IQR = interquartile range, SD = standard deviation, CI = confidential interval *p value calculated using Wilcoxon signed-rank tests, **adjusted p-value calculated using linear regression. Values of blood markers were log transformed and adjustment was made for sex and age.
### Iodine intake

<table>
<thead>
<tr>
<th></th>
<th>TG [µg/L]</th>
<th>52</th>
<th>2.11</th>
<th>87.58</th>
<th>26.98 (± 18.48)</th>
<th>VG (86)</th>
<th>0.39</th>
<th>104.7</th>
<th>29.53 (± 20.82)</th>
<th>0.50</th>
<th>0.79</th>
<th>0.06 (0.01–0.24)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>VN (58)</td>
<td>1.99</td>
<td>345.50</td>
<td>35.33 (± 44.50)</td>
<td>0.12</td>
<td>0.76</td>
<td>0.15 (0.01–0.33)</td>
</tr>
<tr>
<td>AhTGc</td>
<td>[UI/L]</td>
<td>48</td>
<td>1.29</td>
<td>58.90</td>
<td>2.54 (± 8.31)</td>
<td>VG (79)</td>
<td>0.89</td>
<td>298.00</td>
<td>16.24 (± 44.46)</td>
<td>0.01</td>
<td>0.00</td>
<td>0.23 (0.07–0.40)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>VN (40)</td>
<td>0.89</td>
<td>34</td>
<td>13.93 (± 9.16)</td>
<td>0.00</td>
<td>0.00</td>
<td>0.54 (0.32–0.75)</td>
</tr>
<tr>
<td>ATPOc</td>
<td>[UI/L]</td>
<td>48</td>
<td>27.99</td>
<td>535.00</td>
<td>40.41 (± 72.98)</td>
<td>VG (79)</td>
<td>27.99</td>
<td>1.301.00</td>
<td>63.70 (± 200.76)</td>
<td>0.23</td>
<td>0.91</td>
<td>0.11 (0.01–0.27)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>VN (40)</td>
<td>27.99</td>
<td>44.00</td>
<td>30.97 (± 4.82)</td>
<td>0.41</td>
<td>0.25</td>
<td>0.09 (0.01–0.30)</td>
</tr>
</tbody>
</table>

TSH = Thyroid-stimulating hormone, fT4 = free thyroxine, fT3 = free Triiodothyronine, TG = Thyroglobulin, UIC = spot urine iodine, OM = omnivore, VG = vegetarian, VN = vegan, n = number of subjects, IQR = interquartile range, SD = standard deviation, CI = confidential interval *p value calculated using Wilcoxon signed-rank tests, ** adjusted p-value calculated using linear regression. Values of blood markers were log transformed and adjustment was made for sex and age.

#### 3.3. Differences between Dietary Groups in Selected Blood Markers Results

The mean differences in evaluated biomarkers are reported in table (Table 3). We found no significant differences in levels of thyroid-stimulating hormone (TSH), triiodothyronine (fT3), or thyroglobulin (TG) across the groups. There was a very strong statistical difference with a large effect size in anti-thyroglobulin antibodies (AhTGc) between OM vs. VG vs. VN (p < 0.001). Other significant findings were observed in levels of thyroxine (fT4), iodine in spot urine (UIC) between the three groups (OM vs. VG vs. VN) (p < 0.001). Lower values of UIC were observed in VN group compared to the VN group and particularly the OM group. The lowest (5.99 µg/L) but also the highest (991.80 µg/L) levels of UIC were measured in VN subjects. We identified n = 31 VN (41.3%) and n = 31 VG (34.4%) children with iodine deficiency (e.g., UIC < 100 µg/L) (p = 0.06), out of which n = 13 VN (17.3%) and n = 12 VG (13.3%) with mild iodine deficiency (e.g., UIC < 50 µg/L) (p = 0.07) and n = 5 VN (6.1%) and n = 1 VG (1.1%) with severe iodine deficiency (e.g., UIC < 20 µg/L) (p = 0.04). The children with regular iodine supplement use had higher UIC (p < 0.001). Concerning higher levels of ATPOc we retrospectively diagnosed n = 1 children with autoimmune thyroid disease and n = 2 children with suspected autoimmune thyroid disease, these outliers were omitted in data visualisation, (Figs. 3 and 4).

### Discussion

We observed that (1) the mean daily intakes of iodine are significantly lower among VN compared to OM children from the Czech Republic; (2) these differences in take were mirrored by a higher prevalence of the iodine deficiency among VN/ VG children compared to OM children.
Even though iodine intake and status among consumers of plant-based diet are not sufficiently monitored, there are several studies among adults to suggest that vegan and vegetarian diets are risk factors for developing iodine deficiency. These studies consistently describe a lowest UIC among vegans, and the highest among the omnivore people (7, 15–20). In addition, UIC among vegetarians is higher than among vegans yet lower than among omnivorous people (7, 15–18). Similarly, our results from a paediatric population indicate that UIC in vegan children was the lowest followed by vegetarian children and omnivores with the highest UIC. We identified n = 31 VN (41.3%) and n = 31 VG (34.4%) children with iodine deficiency (e.g., UIC < 100 µg/L) (p = 0.06), out of which n = 13 VN (17.3%) and n = 12 VG (13.3%) with mild iodine deficiency (e.g., UIC < 50 µg/L) (p = 0.07) and n = 5 VN (6.1%) and n = 1 VG (1.1%) with severe iodine deficiency (e.g., UIC < 20 µg/L) (p = 0.04). The children with regular use of iodine-containing supplements, tend to have higher UIC (p < 0.001). Of note, none of our study participants had clinical signs of severe iodine deficiency; however, a clinical impact of moderate and mild iodine deficiency could not be properly assessed in the present cross-sectional study.

We observed the highest iodine intake (59.59 µg/day ± 82.18) among the VG group, the lowest in VN group (33.86µg/day ± 39.78), with intermediate intake levels in the OM control group (56.58µg/day ± 38.34). This is in partial agreement with other published studies where vegans tend to have the lowest (21, 22) intake, although some studies show the highest intake of iodine compared to other groups (20, 23), possibly due to excessive seaweed consumption (22–24). Omnivores have the highest estimated average intake of iodine in most studies (9). In one previous study among children, iodine intake was lowest in the vegan group and highest in omnivore group, with intermediate intake levels among vegetarian children (25).

In our study we described a significantly higher prevalence of positive titres of AhTGc in the VN group compared to the VG and OM group; this laboratory parameter is a marker of incipient autoimmune thyroid disease but also described in some studies as a marker of insufficient iodine intake (26–28). The possible long-term results of prolonged mild and moderate iodine deficiency (e.g. mild cognitive impairment, school learning disabilities, autoimmune thyroid disease and others) (5) are yet to be determined using prospective cohort studies.

The overconsumption of algae is linked with the risk of exceeding the limits for iodine daily intake which may lead to thyroid dysfunction. This has been described in some case reports (12, 13), while we did not observe excess iodine consumption via algae in our cross-sectional study (29–33).

A secondary discovery of our analysis, apart the main hypotheses on differences in iodine intake and status, is our description of a higher number of n = 7 VN children with BMI values below the 3rd percentile. Recently published studies performed in a population of children consuming plant-based diets showed that VG/VN children are smaller and more slimmer (34–36).

The diagnosis of iodine deficiency is very difficult, even with many the battery of laboratory tests that we also used in our cross-sectional study. In our population, UIC was the most sensitive marker of iodine status, detecting differences between all three studied groups (e.g., VG, VN, OM). At the same time, TSH, fT4, fT3, and even TG showed to be less or not sensitive at all to detect differences between the three groups, in line with recently published studies (9). However, the significant interindividual and intraindividual variability of UIC measurements in spot urine samples need to be acknowledged (37). This variability can be reduced when correction to serum creatinine is used, although this method is not suitable for correcting UIC values of children nor vegans (38).

One limitation of this study may be its sample size. Nevertheless, we were able to observe significant differences in iodine intake and UIC across the groups, and there are no published previous studies describing an iodine status in vegan or vegetarian children. Our sample was a convenience sample, and we cannot rule out selection bias. A low response rate to our recruitment was observed especially in the adolescent group and the group of parents with very alternative lifestyles. The study may have been affected influence by observation bias because the three-day records were filled out by parents without any control. Nevertheless, three-day records have been shown to provide more accurate nutrient intake data compared to food frequency questionnaires (39). The fact that our results on differences in iodine intake and status across the groups are
highly consistent with previous studies among adults indicates that selection or reporting bias may not have introduced differential measurement error. The non-significant differences in sex, weight, height or BMI and the relative balance between the study groups, are the main strength of our cross-sectional study. It should also be noted that the study contains very detailed data about supplement use, and that the anthropometric measurements were performed on calibrated scales by a trained study nurse. Also, the urine samples were collected as first samples in the morning, and all laboratory analyses were performed immediately after sample collection.

While the knowledge about the necessity of vitamin B12 supplementation seems to be well known among vegans (40) we do not have any information about their iodine status. Therefore, the reason to run this study was a description of iodine saturation, intake, and supplement use in Czech children consuming plant-based diets, and to describe if these children are at possible risk of iodine deficiency, as described reported from cross-sectional studies in adults. Even though the Czech Republic is considered as a country that has solved iodine deficiency as a public health issue (from the year 2004), we have identified a new population at risk, namely children following a vegan and vegetarian diet. Unlike pregnant and lactating women, no attention has been paid to this group so far by public health authorities. Considering the increasing prevalence of plant-based diets, especially in the paediatric population, there is an urgent need for proper guidelines accessible for health professionals for assessing iodine deficiency using suitable markers (40), and the prevention of iodine deficiency via iodine supplementation should be enforced. In this regard, the present research should stimulate an evidence-based discussion concerning medical guidelines and recommendations with a specific focus on the paediatric population consuming plant-based diet in European countries. The possibility of a wide-reaching iodization of plant-based dairy alternatives may be a topic for further discussion.

**Conclusion**

In our cross-sectional study we observed that Czech vegan and vegetarian children are at the risk of iodine deficiency when they rely only on natural sources of iodine while consuming a strictly plant-based diet (e.g., excluding dairy and eggs). It must be stated that we did not observe any consequences of severe iodine deficiency, but many children with biomarker levels indicative of moderate or mild deficiency. On the other hand, we observed more children with positive titres of AhTGc in VN group than in VG or OM group. We further observed that the diet of self-reported vegans was often insufficient in iodine content. Surprisingly the diet of self-reported vegetarians was merely iodine sufficient either, even though it contains dairy and eggs, which are important sources of iodine in our country. Regular use of iodine-containing supplements was associated with significantly higher levels of iodine in spot urine. Apart from our focus on iodine intake and status, a higher number of VN children with lower BMI values, i.e., below the 3rd percentile, was observed. Our observations in a paediatric population are in line with findings from other published studies predominantly carried out among adults (9).

**Declarations**

Data Availability Statement

Datasets used in this study are archived at the institution and can be shared by the author upon reasonable request.

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Author Contributions

MS helped with conceptualization was the lead investigator and wrote the original draft; MH analysed the nutritional intake and wrote the original draft; ES helped with conceptualization and performed the data analysis; AO helped with visualization and with draft editing; JP was lead in resources; TK helped review and edit the original draft; JG organized the
conceptualization, lead the funding acquisition and reviewed the original draft; EE organized the conceptualization, lead the investigation and reviewed the original draft. All authors have read and agreed to the published version of the manuscript.

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Author’s disclosure statements

The authors declare that they have no conflicts of interest. The funders had no role in the study design, collection, analyses, interpretation of data, writing of the manuscript, or the decision to publish the results. The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of Faculty Hospital Královské Vinohrady (protocol code EK-VP/58/0/2019 date of approval 2 October 2019) and Ethics Committee of Third Faculty of Medicine, Charles University in Prague (date of approval 18 October 2019). Informed consent was obtained from all subjects involved in the study and written informed consent has been obtained from the patient(s) to publish this paper.

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**Figures**
Figure 1: Flow Diagram

STROBE Flowchart of a study design
VG = vegetarian, VN = vegan, OM = omnivore, n = number of participants
Figure 2

Mean daily intake of iodine from diet in µg per day

Toddlers = children aged 0–3 years, Schoolers = children aged 3–18 years
**Figure 3**

Iodine in spot urine in µg per litter

UIC = urinary iodine concentration, < 100 µg/L = blue dotted line, < 50 µg/ L = yellow dotted line, < 20 µg/L = red dotted line,
Toddlers = children aged 0-3 years, Schoolers = children aged 3-18 years
Figure 4

Concentration of anti-thyroglobulin antibody
AhTGc = anti-thyroglobulin antibody, positive = red dotted line, Toddlers = children aged 0–3 years, Schoolers = children aged 3–18 years