Iron and Vitamin D Deficiency in Healthy Young Children in Western Europe Despite Current Nutritional Recommendations

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See ''Fe-D Up: Ending Iron and Vitamin D Deficiency in Toddlers'' by Dunn and Goday 519.

ABSTRACT

Background and aim: Iron deficiency (ID) and vitamin D deficiency (VDD) are the 2 most common micronutrient deficiencies in young children worldwide and may lead to impaired neurodevelopment and rickets, respectively. Risk factors for ID and VDD differ between populations. The objective of this study was to determine the prevalence of and risk factors for ID and VDD in 12- to 36-month-old children in Western Europe.

Methods: This study took place in Germany, the Netherlands, and the United Kingdom from 2012 to 2014. A venous blood sample was taken to establish iron and vitamin D status. ID was defined as serum ferritin <12 μg/L in the absence of infection (high sensitivity C-reactive protein <10 mg/L). VDD was defined as serum 25-hydroxyvitamin D <50 nmol/L (20 ng/mL). Furthermore, parents were asked to fill out a questionnaire regarding their child's demographic- and socioeconomic characteristics, food intake, sun exposure, and medical history.

Results: In 325 children (white race 95%, boys 56%, mean age 20.7 months) the overall prevalence of ID and VDD was 11.8% and 22.8%, respectively. The use of primarily cow's milk as major type of milk was associated with ID (odds ratio [OR] 3.20, 95% confidence interval [CI] 1.12–8.53) and VDD (OR 7.17, 95% CI 3.10–16.57). The use of vitamin D supplements (OR 0.20, 95% CI 0.07–0.56) was associated with a lower prevalence of VDD.

Conclusion: Despite current nutritional recommendations, ID and VDD are common in healthy young white children. Health programs focusing on adequate iron and vitamin D intake at an early age should be implemented to prevent deficiencies.

Key Words: cow's milk, formula, iron deficiency, supplements, vitamin D deficiency

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What Is Known

- Iron and vitamin D are common micronutrient deficiencies in young children worldwide.
- In Europe, strategies for the prevention of vitamin D deficiency exist but not for iron deficiency.
- Data on the prevalence of and risk factors for both deficiencies in the white population are scarce.

What Is New

- Iron and vitamin D deficiency are highly prevalent in white children in Western Europe.
- Compliance to vitamin D deficiency preventive strategies (eg, supplementation) is low.
- The use of cow's milk is associated with a higher prevalence of both deficiencies.

Iron deficiency (ID) and vitamin D deficiency (VDD) are the 2 most common micronutrient deficiencies in young children (till 3 years of age) worldwide (1). In Europe, the prevalence of ID in young children varies greatly from 0% to 85% (2) and that of VDD from 0% to 64% (3), depending on the investigated population, nutritional habits, and the definition of ID and VDD that is used. Iron and VDD cause a variety of health issues in children. For example, ID is associated with impaired neurodevelopment (4–7), whereas VDD may lead to the development of rickets (8,9). Furthermore, epidemiological evidence exists of VDD being associated with autoimmune diseases and cancer (3,8).

Guidelines for structural iron supplementation do not exist in European countries. Only in case of proven ID, supplementation of iron is prescribed. Preventive vitamin D supplementation policy does exist, but guidelines differ between countries. For example, in Germany, children without adequate endogenous vitamin D synthesis are recommended to receive 10 to 20 μg vitamin D per day (depending on age) (10). The recommendation in the Netherlands states that all children ages 0 to 4 years should receive 10 μg

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vitamin D per day (both breast- and formula-fed children) (11), whereas British children ages 0.5 to 5 years are recommended to receive only 7 to 8.5 μg vitamin D per day (unless children drink ≥500 mL formula milk) (12). Compliance to these guidelines seems to be low (13).

It is well known that an unbalanced diet can contribute to micronutrient malnutrition (14,15). Other risk factors for micronutrient deficiencies, for example, high skin pigmentation or a low socioeconomic status (16), differ between populations. As risk factors for ID and VDD differ between populations, different (nutritional) strategies may be needed. Current national recommendations may therefore not be adequate to prevent ID and VDD in all children. One should therefore identify risk factors in different clearly defined populations to adjust recommendations and to develop appropriate population-focused (nutritional) strategies to reduce or prevent ID and VDD. In the present study, we therefore investigated the iron and vitamin D status of healthy, mainly white, young children living in highly developed regions of 3 Western European countries. We established the prevalence of ID and VDD in this specific group of children and analysed several known risk factors including food intake details.

METHODS

This study took place in Western Europe from October 2012 to September 2014. Participating countries were Germany (9 private paediatric clinics spread through the country), the Netherlands (Juliana Children's Hospital/Haga Hospital in The Hague, Vrije Universiteit Medical Centre in Amsterdam, and Sophia Children's Hospital/Erasmus Medical Centre in Rotterdam), and the United Kingdom (Royal National Orthopaedic Hospital in London and St Mary's Hospital in Newport, Isle of Wight). The study was approved by the medical ethical review board of all the participating sites. Written informed consent from the parents was obtained for every child.

Inclusion and Exclusion Criteria

Children ages 12 to 36 months and with a stable health status (ie, without any known chronic or recent acute diseases) were eligible for this study. The children were currently drinking milk products with an amount according to national recommendations, that is, ≥300 mL per day (11,17,18). Exclusion criteria were preterm delivery (<32 weeks or <37 weeks with a birth weight <1800 g); known infection during the last week or infection needing medical assistance or treatment during the last 2 weeks; known haemoglobinopathies; any case of anaemia treated in the last 3 months; a blood transfusion received within the last 6 months; the presence of a relevant congenital abnormality; chromosomal disorder or severe disease (eg, tracheoesophageal fistula, tracheomalacia, major congenital heart disease, Down syndrome, HIV, and cancer); having a disorder requiring a special diet (eg, food intolerance or food allergy or complaints such as reflux, constipation and cramps for which a specific diet is required); the current use of anti-regurgitation, anti-reflux, or laxative medication; participation in any other study involving investigational or marketed products concomitantly or within 2 weeks before entering the study; known allergy or intolerance to food components; a vaccination with a live or live-attenuated vaccine received during the last 2 weeks.

Study Procedure

During a hospital or outpatient clinic visit, a venous blood sample was taken and height and weight were measured. In the Netherlands and the United Kingdom, the hospital visit coincided with elective, nonemergency surgery (eg, urological surgeries, inguinal or umbilical hernia operations, or ear-nose-throat procedures), and this procedure has been previously published (19). The blood draw was combined with the placement of an intravenous catheter necessary for administering general anaesthesia. The subjects from Germany where recruited during a regular visit to their paediatrician.

Parents were also asked to fill out a questionnaire regarding their child's demographic- and socioeconomic characteristics, food intake, day care attendance, sun exposure, and medical history. Previously published dietary questionnaires were adapted, translated (in German, Dutch, and English), and used to ask out the food intake (12,19,20). Micronutrient intake was calculated using the Dutch nutrient databank called Nederlands Voedingsstoffenbestand (21). The results reflected the intake in the period of 1 month before the blood draw. A database with electronic case record forms was used to capture all the data.

Definitions and Laboratory Analyses

ID was defined as serum ferritin (SF) <12 μg/L, according to the criteria of the World Health Organization (WHO) (22). Iron deficiency anaemia (IDA) was defined as ID in combination with a haemoglobin concentration <110 g/L, also according to the WHO (22). Ferritin is an acute phase protein that may increase when an infection is present, even in the presence of low iron stores. Therefore, high sensitivity C-reactive protein (hsCRP) was also determined in the venous blood sample. All the children with elevated hsCRP concentrations (≥10 mg/L) were excluded from the analyses regarding ID and IDA. VDD was defined as serum 25-hydroxyvitamin D (25(OH)D) <50 nmol/L (20 ng/mL), as this is the cutoff level recommended by most experts including the ESPGHAN Committee on Nutrition (3,8,23). It is known that seasonal variation in circulating 25(OH)D concentrations is large relative to mean values. Therefore, we also calculated subject-specific mean annual 25(OH)D concentrations from single values, by using the cosinor model by Sachs et al (24).

SF and serum 25(OH)D were analysed by using an Abbott Architect i2000 immunology analyser with a chemiluminescent immunoassay method and a chemiluminescent microparticle immunoassay method, respectively. hsCRP was analysed using an Abbott Architect c16000 clinical chemistry analyser with a turbidimetry method.

Statistical Analysis

The statistical analyses were performed using Statistical Package for the Social Sciences (version 21.0; SPSS Inc, Chicago, IL). To assess the prevalence of ID or IDA, we analysed complete blood samples of children with nonelevated hsCRP levels. Univariate analyses of characteristics were performed using a Student *t* test for normally distributed continuous variables and a χ^2 test for dichotomous variables, for comparison of groups. In case of a nonnormal distribution, we used Mann–Whitney tests to compare medians between groups. To analyse risk factors for ID and VDD, we calculated odds ratios (ORs) with 95% confidence intervals (CIs). Finally, we performed binary logistic regression analyses to correct for possible confounders. These possible confounders were based on biological principals (eg, sex and age) and previously reported associations (eg, supplement use, type of milk, and sun exposure) (Fig. 1) (3,8,16,19,25). Statistical significance was defined as $P < 0.05$.

RESULTS

Study Population

The study population consisted of 325 children: 268 from Germany (82.5%), 45 from the Netherlands (13.8%), and 12 from

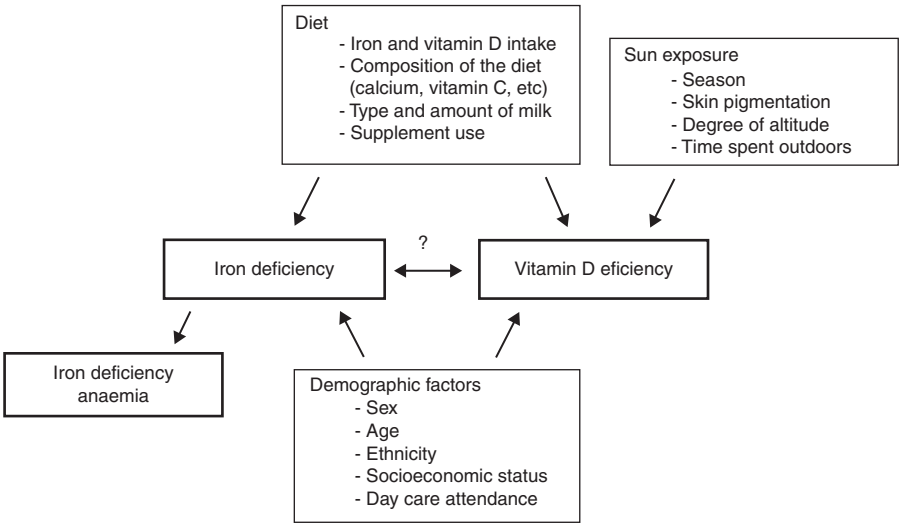

FIGURE 1. Causal diagram for iron and vitamin D deficiency.

the United Kingdom (3.7%). As earlier described, the German children were recruited in 9 different paediatric clinics spread through the entire country: Nürnberg (n = 17 children), Baunatal (n = 3), Detmold (n = 46), Erfurt (n = 48), Kleve (n = 24), Bramsche (n = 37), Gilching (n = 9), Berchtesgaden (n = 73), and Kirchheim-Heimstetten (n = 11). The majority of the children were from the white race (94.8%). The percentage of white children is higher than in general in the participating countries because most children were recruited in well-developed urbanized areas. White people are predominantly living in these specific areas. Moreover, children were excluded if the investigator was uncertain about the ability of the parents to comply with the protocol requirements. Subsequently, children were excluded if their parents did not understand German, Dutch, or English. The mean age of the children was 20.7 months (±7.6 months), and 56.3% were boys (Table 1). Other characteristics of the study population are shown in Table 1.

Food Intake

About two thirds (64.0%) of the children were either exclusively or partially breast-fed at some stage, with a mean breast-feeding duration of 5.5 months (±4.1 months). Almost all the children had received formula or were still being formula fed (90.8%). At the time of the blood draw, 51.1% of the children received primarily young child formula (commercially available formula for children 1–3 years of age), whereas 44.0% used primarily cow's milk. The average volume of milk per day was 515 mL (±226 mL) (Table 2). This amount was comparable for young child formula users and cow's milk users ($P > 0.05$, data not shown). More than 400 mL milk was given to 20.6% of the cow's milk users and to 27.1% of the young child formula users (Table 2).

Only 5 children (1.5%) used supplements containing iron, whereas 93 children (28.6%) used supplements containing vitamin D (Table 2). The percentage of children receiving vitamin D

TABLE 1. Characteristics of the study population (n = 325)

	Mean or number	SD or percentage
Demographic		
Age, mo	20.7	SD 7.6
Male sex, %	183	56.3%
White race, %	308	94.8%
Highest educational level of either parent, %*		
Primary school	51	15.7%
High school/trade school	149	45.8%
University	66	20.3%
Professional status of parents, %*		
≥1 working	247	76.0%
None working	11	3.4%
Other		
Gestational age, wks	38.9	SD 1.7
Birth weight, g	3319	SD 548
Day care attendance, %	143	44.0%
≥1 hour spent outside per day, %	252	77.5%
Use of sunscreen or protective clothing, %	90	27.7%

Data are expressed as means (with standard deviation) or numbers (with percentage). SD = standard deviation.
* Because of missing data, not all numbers add up to 100%.

TABLE 2. Nutrition details of the study population (n = 325)

	Mean or number	SD or percentage
History		
Ever breast-fed, %*	208	64.0%
Breast-feeding duration, mo*	5.5	SD 4.1
Ever formula fed, %*	295	90.8%
Age of introduction of solid foods, mo	5.6	SD 1.9
Main type of milk intake during previous month		
Use of primarily cow's milk, %	143	44.0%
Use of >400 mL cow's milk per day, %	67	20.6%
Use of primarily formula, %	166	51.1%
Use of >400 mL formula per day, %	88	27.1%
Amount of milk per day, mL	515	SD 226
Supplements		
Use of supplements containing iron, %†	5	1.5%
Use of supplements containing vitamin D, %†	93	28.6%
Iron		
Iron intake from milk, mg/day‡	3.0	0.0–5.2
Iron intake from food, mg/day‡	4.4	2.8–6.1
Intake of haem iron from food, mg/day‡	0.2	0.1–0.3
Intake of nonhaem iron from food, mg/day‡	4.1	2.7–5.8
Iron intake below EAR of 3 mg/day, %	58	17.8%
Vitamin D		
Vitamin D intake from milk, μg/day‡	4.4	0.0–6.6
Vitamin D intake from food, μg/day‡	0.8	0.4–1.2
Vitamin D intake below EAR of 8 μg/day, %	194	59.7%

Data are expressed as means (with standard deviation) or numbers (with percentage), unless otherwise noted. SD = standard deviation; EAR = estimated average requirement (the expected amount of micronutrient that will satisfy the needs of 50% of the children).

* Exclusively or partially.

† Also during the week before entering into the study.

‡ No normal distribution, and therefore we report the median with IQ25–IQ75.

supplementation by country was 48.9% in the Netherlands, 25.7% in Germany, and 16.7% in the United Kingdom. The mean (reported) iron and vitamin D intake from supplements in those consuming supplements was 5.7 mg (±5.6 mg) and 11.0 μg (±3.1 μg) per day, respectively.

The median iron intake from milk and food (both haem and nonhaem iron) were 3.0 and 4.4 mg/day, respectively (Table 2). The main food categories that contributed to the iron intake from food were vegetables (34%), breakfast cereals (26%), bread (18%), and meat (10%) (data not shown). The median vitamin D intake from milk and food were 4.4 and 0.8 μg/day, respectively (Table 2). In addition to milk, butter products (33%) and breakfast cereals (33%) also accounted for the biggest share in vitamin D intake (data not shown).

Prevalence of ID and VDD

Twenty children had an elevated hsCRP and were therefore excluded from the analyses regarding ID and IDA. Ferritin concentrations were missing in another 16 children (4.9%). In the remaining 289 children, the mean SF concentration was 29 μg/L (±18 μg/L, range 1–97 μg/L). The mean serum 25(OH) vitamin D concentration was 68.5 nmol/L (±26.0 nmol/L, range 18–151 nmol/L [27.4 ng/mL, range 7.2–60.5 nmol/L]) and was missing in 17 children (5.2%). The overall prevalence of ID and VDD was 11.8% and 22.8%, respectively. Twelve children (3.9%) had IDA. Subgroup analyses revealed a higher prevalence of both ID and VDD at a higher age. The prevalence of ID was 11.2% in children from 1 to 2 years and 14.9% in the group of children ages 2 to 3 years ($P = 0.366$). For VDD, the prevalence increased from 16.3% in children from 1 to 2 years to 38.7% in the group of children ages 2 to 3 years ($P < 0.001$). A total of 5.9% of the children in our study population had both ID and VDD.

More children (59.1%) were recruited during the fall/winter (September–February). The VDD prevalence was lower in children recruited during fall/winter compared with children recruited during spring/summer (18.6% vs 31.3%, $P = 0.010$).

The VDD prevalence, while using the subject-specific mean annual 25(OH)D concentrations, was comparable with the prevalence while using the single vitamin D concentrations (22.5% instead of 22.8%).

Risk Factors for ID

Demographic (age, sex and race) and socioeconomic characteristics (educational level and working status of parents) did not differ between children with and without ID. The percentage of children attending day care was also similar for both groups. ID was associated with the use of primarily cow's milk, especially in the case of consuming >400 mL per day (Table 3). The prevalence of ID in children who received mainly young child formula was 5.4%, whereas in children receiving mainly cow's milk this was 19.7% ($P < 0.001$).

Remarkably, the children with ID had a higher (total) iron intake from food (with exclusion of drinking cow's milk and/or formula) than the children with an adequate iron status. This was merely because of a higher intake of nonhaem iron from food (Table 3).

TABLE 3. ID: univariate and multivariate analyses

	Univariate analysis				Multivariate analysis			
	Beta	*P*	OR	95% CI	Beta	*P*	OR	95% CI
Demographic factors								
Age, mo	0.043	0.065	1.04	1.00–1.09	−0.002	0.962	1.00	0.93–1.07
Male sex	0.222	0.543	1.25	0.61–2.55	0.311	0.455	1.37	0.60–3.09
Nonwhite race	−0.791	0.451	0.45	0.06–3.54				
≥1 parent with university education	0.124	0.774	1.13	0.49–2.63	−0.004	0.994	1.00	0.35–2.86
≥1 working parent	−0.710	0.061	0.49	0.23–1.03				
Day care attendance	0.443	0.221	1.56	0.76–3.16	0.126	0.774	1.13	0.48–2.68
Nutrition								
Breast-feeding duration, mo[†]	0.148	0.054	1.16	1.00–1.35	0.128	0.142	1.14	0.96–1.35
Current type of milk: cow's milk	1.197	0.002*	3.31	1.56–7.02	1.162	0.020*	3.20	1.12–8.53
Use of >400 mL cow's milk per day	0.856	0.025*	2.35	1.11–4.97				
Use of iron supplements[‡]	0.598	0.598	1.82	0.20–16.76	0.460	0.717	1.58	0.13–19.10
Iron intake from food, mg/day	0.113	0.029*	1.12	1.01–1.24	0.108	0.050	1.12	1.00–1.24
Intake of haem iron from food, mg/day	−0.502	0.626	0.61	0.08–4.55				
Intake of nonhaem iron from food, mg/day	0.131	0.022*	1.14	1.02–1.28				

ID = iron deficiency; OR = odds ratio; CI = confidence interval.
[†] Exclusively or partially.
[‡] Also during the week before entering into the study.
* Statistically significant with $P < 0.05$.

Binary logistic regression analysis was performed with ID as dependent variable and the following covariates added: age, sex, university education, breast-feeding duration, day care attendance, the use of iron supplements, iron intake from food, and the use of cow's milk. This multivariate analysis showed that the present use of cow's milk was associated with a higher prevalence of ID (OR 3.20, 95% CI 1.12–8.53) (Table 3).

Risk Factors for VDD (Based on the Mean Annual Vitamin D Concentrations)

The children with VDD were significantly older, were more frequently male, and attended more frequently day care. They received less frequently vitamin D supplements and were more used to receive cow's milk, in comparison with children without VDD (Table 4). The prevalence of VDD in children who received mainly young child formula was 5.7%, whereas this was 43.6% in children receiving mainly cow's milk ($P < 0.001$).

Binary logistic regression analysis was performed with VDD as dependent variable and the following covariates added: age, sex, university education, breast-feeding duration, day care attendance, ≥1 h/day spent outside, the use of vitamin D supplements, vitamin D intake from food, and the use of cow's milk. This multivariate analysis showed that the present use of cow's milk was associated with a higher prevalence of VDD (OR 7.17, 95% CI 3.10–16.57), whereas the use of vitamin D supplements (OR 0.20, 95% CI 0.07–0.56) was associated with a lower prevalence of VDD (Table 4).

TABLE 4. VDD: univariate and multivariate analyses

	Univariate analysis				Multivariate analysis			
	Beta	*P*	OR	95% CI	Beta	*P*	OR	95% CI
Demographic factors								
Age, mo	0.114	0.000*	1.12	1.08–1.16	0.033	0.261	1.03	0.98–1.10
Male sex	0.713	0.013*	2.04	1.16–3.58	0.385	0.123	1.47	0.98–3.17
Nonwhite race	0.074	0.900	1.08	0.34–3.45				
≥1 parent with university education	−0.655	0.080	0.52	0.25–1.08	−0.536	0.333	0.59	0.20–1.73
≥1 working parent	−0.519	0.086	0.60	0.33–1.08				
Day care attendance	0.584	0.031*	1.79	1.06–3.05	0.281	0.445	1.33	0.64–2.73
≥1 hour outside per day	0.624	0.111	1.87	0.87–4.02	−0.168	0.741	0.85	0.31–2.29
Nutrition								
Breast-feeding duration, mo[†]	0.010	0.894	1.01	0.87–1.17	−0.036	0.714	0.97	0.80–1.17
Current type of milk: cow's milk	1.970	0.000*	7.17	3.87–13.30	1.970	0.000*	7.17	3.10–16.57
Use of >400 mL cow's milk per day	1.544	0.000*	4.68	2.58–8.49				
Use of vitamin D supplements[‡]	−1.646	0.000*	0.19	0.08–0.44	−1.636	0.002*	0.20	0.07–0.56
Vitamin D intake from food, mg/day	−0.012	0.898	0.99	0.83–1.18	−0.080	0.500	0.92	0.73–1.64

VDD = vitamin D deficiency; OR = odds ratio; CI = confidence interval.
[†] Exclusively or partially.
[‡] Also during the week before entering into the study.
* Statistically significant with $P < 0.05$.

DISCUSSION

In this study, we have found that ID and VDD are highly prevalent in otherwise healthy, predominantly white, young children living in well-developed regions in 3 Western European countries. We have also found that ID and VDD coexist in 5.9% of this population. The use of vitamin D supplements is associated with a lower prevalence of VDD, but implementation of a national program seems problematic because only 16.7% to 48.9% of the children received supplements while in all participating countries programs exist. Furthermore, we have demonstrated that the use of cow's milk is associated with a higher prevalence of ID and VDD. Factors like perinatal and socioeconomic characteristics did not influence the prevalence of both deficiencies.

Despite having investigated healthy young children in well-developed regions in Western Europe, the overall prevalence of ID and VDD was high (11.8% and 22.8%, respectively). Other studies in similarly aged children from Western European countries reported prevalence rates of ID between 2.8% and 31% (2). The great variation could be explained by different definitions of ID that were used. There is no consensus about which definition is best, and therefore we used the criteria of the WHO for ID. A Dutch study among almost similarly aged children used the same diagnostic criteria for ID and found a prevalence of 18.8% (19). The lower prevalence of ID in our study can be explained by the homogeneity of our population. It is known that a nonwhite race is associated with an increased prevalence of ID (8). Our study population consisted of predominantly white toddlers (94.8%), whereas the percentage of white children in the Dutch study was 69.2% (19).

Limited data are available on the prevalence of VDD in young European children (<3 years). Existing studies report overall prevalence rates of 0% to 64% in paediatric populations with a wider age range (3). Comparison of these studies is, as for ID, hampered by different definitions of VDD that were used. There is no evidence-based guideline about which cutoff levels of 25(OH)D indicate sufficiency, deficiency, or toxicity. The Institute of Medicine and the Endocrine Society state that practically all persons are vitamin D sufficient at serum 25(OH)D levels of ≥50 nmol/L (20 ng/mL). Serum concentrations >75 nmol/L (30 ng/mL) are not consistently associated with increased health benefit (26,27). Because of the lack of an evidence-based guideline, we decided to use 25(OH)D serum concentrations <50 nmol/L (20 ng/mL) to define VDD according to the recommendations of the ESPGHAN Committee of Nutrition (3). Furthermore, another important issue is that the seasonal variation in circulating 25(OH)D concentrations is large relative to mean values. Subsequently, single measurements may misclassify year-long vitamin D status. Not taken this into account can lead to imprecision and bias in studies. To prevent bias in our study, we performed additional analyses after using a cosinor model that estimates subject-specific mean annual 25(OH)D concentrations from single values. The prevalence of VDD, while using this mean annual vitamin D concentrations, was similar. However, we need to realize that the model of Sachs et al (24) was developed from data of adult patients from the Multi-Ethnic Study of Atherosclerosis from the United States. We do not know whether the model can be generalized from these adults to young healthy white children in Western Europe.

Consistent with previously published studies, we found that the use of cow's milk is associated with a higher prevalence of ID (19,25). In contrast to our results, however, the use of cow's milk has been shown to be associated with higher 25(OH)D levels (28,29). In some countries, such as Canada where the aforementioned studies took place, milk is fortified with vitamin D (30). This may explain the finding of higher vitamin D levels among cow's milk users in these studies, whereas cow's milk is not fortified with vitamin D in the regions that we have studied. Furthermore, it is known that full fat cow's milk has higher vitamin D content than semiskimmed cow's milk. Because only 65% of the cow's milk users in our study received full fat cow's milk (data not shown), we speculate that in the other studies more children may have received full fat cow's milk.

It is remarkable that the iron intake from food was higher in the children with ID than in those with an adequate iron status, although this association was not seen after performing multivariate analysis. It is known that the bioavailability of iron depends on the composition of the diet. Food products containing haem iron (eg, meat and fish) are better absorbed than those containing nonhaem iron (eg, vegetables). Furthermore, several factors enhance (eg, vitamin C) or inhibit (eg, calcium) iron absorption. Unfortunately, we do not have data on vitamin C intake in our study population. We do know that children with ID in our study, however, used more cow's milk than those without ID. Cow's milk has not only a low iron content but also contains calcium that inhibits iron absorption.

Day care attendance did not affect the presence of ID or VDD in our study population, although 2 other studies have found that preschool/day care attendance was associated with a lower prevalence of ID (16,19). It is thought that children eat more (or food of better nutritional quality) at preschool/day care because of meals that are collectively used on structural moments with more time and attention for eating (19). The aforementioned studies took place in the United States and the Netherlands. It is possible that feeding habits and nutritional quality at German and British day care centres are different from those in the United States and the Netherlands and therefore do not influence the prevalence of both micronutrient deficiencies.

We found that the use of vitamin D supplements was associated with a lower prevalence of VDD. The ''protective effect'' of vitamin D supplementation on VDD (rickets) has been previously reported (3,8). The ESPGHAN Committee on Nutrition states that vitamin D is essential for bone health in infants, children, and adolescents. The committee advices national authorities to adopt policies aimed at improving vitamin D status by measures such as vitamin D supplementation, depending on local circumstances (3). New policies or a more strict focus on the use of supplements is necessary because less than half of the children in our study population used vitamin D supplements.

We did not find an association between VDD and ethnicity or sun exposure (measured as on average ≥1 h/day spent outdoors), although previous studies have reported skin pigmentation and limited sun exposure as risk factors for VDD (3,8,9,23,31). The lack of a relation between VDD and these variables in our study may be explained by the very low number of children of nonwhite ethnicity. Furthermore, our method to establish ultraviolet (UV) exposure may not have been discriminative enough. The amount of UV exposure available for the synthesis of vitamin D depends on more factors than time spent outdoors, such as the amount of skin pigmentation, body mass, degree of altitude, the amount of skin exposed, and the extent of UV protection, including clothing and the use of sunscreen (31). However, as mentioned before, we used mean annual vitamin D concentrations for our analyses to adjust for the month that the vitamin D status was determined.

Surprisingly, we found a lower prevalence of VDD in the children who were recruited during fall/winter. This can be explained by the fact that these children spent a longer time (≥1 hour) outside per day than the children recruited during spring/summer (25.3% vs 10.3%, $P = 0.001$), although they probably wear more clothing during fall/winter that limits UV exposure. It is also possible that the children recruited during the beginning of the fall still have an adequate vitamin D status from the summer.

The difference in prevalence is not explained by a difference in supplement use during the seasons (data not shown).

A small number of children in our study had both ID and VDD. The coexistence of both micronutrient deficiencies has only been previously described in Korean children and adolescents (32,33), and could be explained by poor nutritional habits in general. Several mechanisms for the coexistence of VDD and IDA have been proposed. On one hand, vitamin D is suggested to increase the storage and retention of iron by reducing the activity of proinflammatory cytokines that inhibit iron absorption. On the other hand, ID impairs the intestinal absorption of fat and vitamin A and thereby maybe also the absorption of vitamin D (33,34).

The strength of our study is that we investigated a homogenous population with similar socioeconomic characteristics and genetic background. In this way, we were able to look at the influence of nutrition on the iron and vitamin D status of young white children in Western Europe. On the contrary, the homogeneity may also hamper generalization of our results and conclusions to nonwhite children and children living in other parts of Europe. More epidemiological studies in other European countries are necessary to determine risk factors in these populations.

A limitation of our study could be our assessment of the food intake. Food frequency questionnaires have their limitations to assess nutrient intake because it is a retrospective method to collect the food intake during a previous time frame. However, literature also states that these kind of questionnaires have been found suitable for determining iron and vitamin D intake in infants and pre-scholars (35) and therefore we believe that our conclusions are valid.

The majority of our study population consists of German children (82.5%). We hypothesized that different nutritional habits in each country, and not the country per se, could have led to a different micronutrient intake and therefore another deficiency prevalence. Subgroup analyses showed similar results, however, regarding micronutrient intake and prevalence of ID and VDD in the German and non-German children (data not shown). Hence, we do not think that the overrepresentation of German children is a limitation of our study.

CONCLUSION

We have shown that ID and VDD are highly prevalent in a homogeneous population of healthy young white children living in Western Europe. As expected, supplementation of vitamin D is associated with a lower prevalence of VDD, but only a minority of the children received supplements. The use of cow's milk is associated with a higher prevalence of both ID and VDD. Current nutritional recommendations and habits are apparently insufficient in the prevention of ID and VDD, even in healthy white children. New strategies should focus on the composition of the diet and/or consider the use of fortified products because compliance to current supplementation policies is low.

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