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Higher Prevalence of Vitamin D Deficiency Is Associated with Immigrant Background among Children and Adolescents in Germany[1,2]

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[6] Abbreviations used: KiGGS, German National Health Interview and Examination Survey for Children and Adolescents; CAPI, computer assisted personal interview; 25(OH)D, 25-hydroxyvitamin D; OR, odds ratio; PTH, parathyroid hormone.
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Abstract

In recent years, a high prevalence of vitamin D deficiency among children and adolescents has been reported in countries with moderate climates. Those with an immigrant background living under these conditions are at especially high risk. To date, representative data in Germany is lacking. We analyzed 25-hydroxyvitamin D [25(OH)D] concentrations of 10,015 children and adolescents, aged 1–17 y, who participated in the German National Health Interview and Examination Survey for Children and Adolescents. The proportion of immigrants was 25.4%, corresponding well to their percentage of the population. Among 3- to 17-y-old participants, 29% of immigrant boys and 31% of immigrant girls had 25(OH)D concentrations ,25 nmol/L (severe to moderate vitamin D deficiency) compared with 18% of nonimmigrant boys and 17% of nonimmigrant girls. Furthermore, 92% of immigrant boys and 94% of immigrant girls had 25(OH)D concentrations ,75 nmol/L (levels above 75 nmol/L are defined as optimal regarding various health outcomes) compared with 87% of nonimmigrants. Boys with a Turkish or Arab-Islamic background had an increased risk of having 25(OH)D concentrations ,25 nmol/L compared with nonimmigrants (odds ratio [OR] 2.3; [95% CI] 1.4–3.8 and OR 7.6; [95% CI] 3.0–19.1). The same was true for girls with a Turkish (OR 5.2; [95% CI] 2.9–9.6), Arab-Islamic (OR 5.9; [95% CI] 2.5–14.0), Asian (OR 6.7; [95% CI] 2.2–19.8), or African (OR 7.8; [95% CI] 1.5–40.8) background. Supplementation of vitamin D beyond infancy, especially in high-risk groups, or fortification of food should be considered. J. Nutr. 138: 1482–1490, 2008.

Introduction

Vitamin D is a steroid hormone with pleiotropic effects on calcium and phosphorus metabolism and the immune system. The clinical outcomes of a severe vitamin D deficiency are rickets in children and osteomalacia in adults. However, even milder states of deficiency have recently been implicated in the pathogenesis of diabetes mellitus and other chronic diseases involving low-grade chronic inflammation (1–3). In western countries, severe vitamin D deficiency is rarely observed, whereas milder deficient states are more common. Studies from various countries have indicated that individuals with an immigrant background living in Western European countries (4–9), the United States (10,11), Canada (12), Australia (13,14), or New Zealand (15,16) seem to be at particularly high risk of vitaminDdeficiency. This finding may stem from a number of reasons, including lower vitamin D intake, pigmented skin, and limited exposure to sunshine due to cultural dress codes (e.g.
veiling) or less time spent outdoors (17,18). A continuous migration to Germany has occurred since the early 1960s, especially from Southern European countries and from Turkey. Currently, .25% of people with an immigrant background in Germany are of Turkish origin. A recent study among Turkish people has shown a high prevalence of vitamin D deficiency in this group independent of whether they lived in Turkey or Germany, especially in veiled women (5). It is now increasingly recognized that vitamin D deficiency not only affects adults but to a large extent even children and adolescents with an immigrant background (19). In Germany, the intake of vitamin D supplements (10–12.5 mg/d) is recommended during infancy to avoid rickets (starting at the end of the first week, continuing until the age of 1 y and also during the 2nd winter for children born in the sun-deprived months). The German National Health Interview and Examination Survey

for Children and Adolescents (KiGGS)6 is the first study to provide information on the health status of children and adolescents in Germany at the national level. The aimof this study was to compare the prevalence of vitamin D deficiency between immigrants and nonimmigrants aged 1–17 y in Germany, taking into account the recommended vitamin D supplementation during infancy. Furthermore, we identified independent determinants of vitamin D concentrations among immigrants and determined groups at high risk of vitamin D deficiency.

Methods

Study population. KiGGS is a representative survey of children and adolescents aged 0–17 y, conducted fromMay 2003 toMay 2006.Based on a 2-staged clustered design, stratified by federal state and community size, anage-stratifiedrandomsamplewas drawnfromlocal populationregistries (20). To enable separate analyses of East andWest Germany, a disproportional number of sample points was included to represent formerWest and East Germany. At an overall relative participation of 66.6%, the study population comprised 17,641 participants. Overall, 25.4%of the children and adolescents had an immigrant background, corresponding well to current population statistics regarding the immigrant fraction of the German population in the respective age groups (28.6% of 0- to 18-y-old boys and girls) (21). The study was approved by the Charite´ Berlin ethics committee. Participants beyond 14y of age andall parents providedwritten informed consent prior to the interview and examination (20). From the total study population, we excluded survey participants seen during the first year of the study (n ¼ 4366) due to a change in laboratory method. Furthermore, we excluded children younger than 1 y
of age (n ¼ 935) from whom blood samples were generally not obtained, as well as children whose parents or caregivers declined venipuncture (n ¼ 2319). Another 6 study participants were excluded due to invalid measurements. Thus, the present analysis is based on 10,015 participants
1–17 y of age, for whom valid measures of serum 25-hydroxyvitamin D [25(OH)D] concentrations were available. As mainly younger children or their parents declined to give a blood sample, the mean age differs between KiGGS participants with and without blood samples. Data collection. Data collection comprised age-specific standardized self-administered parent questionnaires, physical examinations and tests, as well as a computer assisted personal interview (CAPI) for parents and caregivers. The CAPI was conducted by specifically trained study physicians to collect detailed information on medical history, vaccination status, and medication use. Questionnaires and tests differed slightly for children 1–2, 3–6, 7–10, 11–13, and 14–17 y of age to address health issues specific to the main developmental stages of childhood and adolescence. Questionnaire differences applied to questions regarding breast-feeding practices, physical activity, media consumption, and sexual maturation, among other things. Information on food intakewas collected with a self-administered FFQ, covering questions about the frequency of food intake and usual portion sizes of common food groups (20). Blood samples from nonfasting subjects were obtained and immediately processed and separated. Extra serumwas aliquoted and stored at240_C. Laboratory assay. We measured serum 25(OH)D, because it represents the best indicator of vitaminDstatus. In y 1 of the survey, serum 25(OH)D
was determined by enzyme immunoassay. However, quality assessment revealed stability problems, requiring a change in themethod. A LIAISON chemiluminescence immunoassay, CLIA (DiaSorin) was chosen; subsequently, validmeasurementswere completed for a total of 10,015 children and adolescents. Inter- and intra-assay CVwere 11.7 and 9.9%. The lower detection limit of the assay was 5 nmol/L (22). We found no significant differences in age or any of the main study characteristics between participants in the 2 different laboratory measurement methods. Operationalization of study variables. Vitamin D status was primarily categorized, using 25(OH)D cut-off points according to Lips (23): severe vitamin D deficiency (,12.5 nmol/L), moderate vitamin D deficiency (12.5–25 nmol/L), mild vitamin D deficiency (25–50 nmol/L), and safe reference limit (.50 nmol/L). Recent studies suggest an even higher threshold of 75 nmol/L for maximal parathyroid hormone (PTH) suppression and optimal health (24). A child was defined as having an immigrant background if at least 1 of the child's parents was not born in Germany and/or had no German citizenship, including both children and adolescents with a 1- and a 2-sided immigrant background (21). For multivariate analyses, this variable was further differentiated. To allow for types of skin pigmentation, we tried to categorize immigrants' countries of origin under geographical aspects. Furthermore, cultural and religious as well as lifestyle aspects were taken into account. We considered primarily the mother's country of origin (in cases where this information was lacking, the father's country of origin was considered). Countries were then grouped as follows: Turkey, Arab-Islamic countries, Eastern countries (Central and Eastern Europe and former Soviet Republics), Southern European countries, Western countries (USA, Canada, and Western
Europe), Latin-America, Asia, Africa, and other countries. Arab-Islamic countries include the following countries: Lebanon, Morocco, Algeria, Iraq, Egypt, Pakistan, Syria, Jordan, Senegal, Tunisia, Brunei,

Indonesia, Iran, Kuwait, Bangladesh, Guinea, and Gambia. The remaining African countries (without Arab-Islamic majorities) are summarized into African countries. As Turkey is the main country of immigration in Germany, we included Turkey in our analyses separately. To assess the degree of integration of immigrants, we developed an index using information on German language abilities, status of parents' occupation, school performance, social integration, and residence permit status. Immigrants, whose residence permit status was limited in time and insecure to renew, were defined as having a low degree of integration. The same was true for those with low scores of 3 of the 4 remaining categories (German language abilities, status of parents' occupation, school performance, and social integration). Otherwise, showing high scores of 2 (or 3) of 4 categories was defined as a middle (or high) degree of integration. Using information on parents' education, occupation, and household income, we also constructed an index of socioeconomic status (25). Community size was defined as nonmetropolitan (,100,000 habitants) or metropolitan ($100,000 habitants). Information on the use of either vitamin D or calcium supplements during 7 d before the examination was derived from the CAPI. In addition, the use of vitamin D and calcium supplements (yes/no) was queried in the FFQ. These data were combined, resulting in dichotomous variables. Participants were classified into age-specific tertiles of physical activity as well as media consumption (reported number of hours per week spent watching TV/ videos, sitting at the computer, and playing on a game console). The categorization of physical activity was based on information regarding leisure time physical activities: engagement in sports with or without a sports club (among 3- to 10-y-old children) and being involved in sweatinducing activities (among 11- to 17-y-old participants). BMI was calculated by dividing weight (kg) by squared height (m). BMI was categorized into age- and gender-specific percentiles for children and adolescents: obese (.97th), overweight (90th–97th), underweight (3rd– 10th), and severely underweight (,3rd), indicating reference values generally used in Germany (26). We also computed predicted body fat using skin fold equations according to Slaughter (27). Development and relative validation of the vitamin D and calcium intake indexes. In KiGGS, food intake was assessed with a selfadministered FFQ, including frequencies and usual portion sizes of 45 food groups (28). This method does not allow a precise estimate of nutrient intake. We therefore obtained additional information on food and nutrient intake in the KiGGS module EsKiMo, a special module (indepth study) of the KiGGS core survey, including a random subsample of 2506 participants 6–17 y of age. Among 6- to 11-y-old children, dietary intake was assessed by 3-d food diaries completed by parents, whereas a computer-assisted modified dietary history (DISHES) with documented validity (29) was administered to 12- to 17-y-old participants. The EsKiMo module was conducted between January and December 2006. To allow a comparison with the KiGGS core survey, EsKiMo participants 12–17 y of age were asked to fill in the KiGGS FFQ once again (30).

Based on the FFQ data of the KiGGS core survey, both a vitamin D intake index and a calcium intake index were constructed by multiplication of food frequencies and portion sizes as well as the nutrient contents using the German Food Composition database (BLS, Version 2.3). Participants were grouped into tertiles of the indices. According to their relevance of contribution, the following foods were included in the vitamin D intake index: fish, milk, yoghurt, cheese, curd cheese, cream cheese, pancakes, mayonnaise, eggs, margarine, and butter. The vitamin D content of fatty fish vs. lean fish differs substantially. Therefore, we obtained an average estimate of vitamin D intake deriving from fish consumption using data from the EsKiMo module and included it in the vitamin D intake index. The foods milk, juice, tap water, mineral water, cereals, whole-grain bread, white bread, cheese, curd cheese, cream cheese, cake, and biscuits were included in the calcium intake index. Using data from 1249 participants of the EsKiMo module, aged 12– 17 y (with both a valid FFQ and DISHES interview), quintiles of the indices were validated against quintiles of vitamin D and calcium intakes derived from the DISHES interview. Percentage of agreement, defined as proportion of participants falling into the same or adjacent quintile, was 70% for vitamin D and 68.4% for calcium. Gross misclassification (falling into opposite quintiles) was 2.5% for vitamin D and 2.4% for calcium. Spearman correlation coefficients for cross-validated categories were 0.43 (P , 0.001) for vitamin D and 0.40 (P , 0.001) for calcium, similar to those reported in previous validation studies (31,32).

Statistical analyses. The data were analyzed using SAS version 9.1 software (SAS Institute) and SPSS version 14.0 software (SPSS GmbH Software) for complex survey design analyses. Analyses were based on combined age stratifications as used for data collection (age groups: 1–2 y and 3–17 y). A P-value of # 0.05 was considered significant based on 2-sided tests. To ensure that the results were representative at the national level, a specific weighting factor was applied to all statistical analyses. The weighting procedure mainly intends to correct for sampling design (disproportionately higher sample size in East vs. West Germany) as well as for deviations between the actual study sample and German population statistics (as of December 31, 2004) based on crossclassifications by age, sex, residence in West or East Germany, and nationality. The weighting factor also corrects discrepancies due to the reduced sample size of individuals with valid 25(OH)D measurements. We only report weighted results throughout the manuscript. Sex-specific group differences in categorical variables between participants with,

and without, an immigrant background were tested using the chi-square test statistic (adjusted F-value for the Wald loglinear chi-square statistic). We estimated multiple linear regression models for immigrants with vitamin D concentrations as the dependent variable. The association between immigrant status (including specific subgroups) and severe to moderate vitamin D deficiency (,25 nmol/L) was assessed in multiple logistic regression models by gender, adjusting for age and season of examination as well as for further relevant covariates (socioeconomic status, residence in East Germany, living in nonmetropolitan areas, vitamin D supplement use, vitamin D and calcium intake index, BMI groups, physical activity, and media consumption). ''Other immigrants'' were excluded in this analysis, as this subgroup was very small and heterogeneous. Results In both sexes, participants with an immigrant background (aged 1–17 y) showed a significantly lower socioeconomic status and were also significantly less likely to live in East Germany or in nonmetropolitan areas compared with nonimmigrants (Table 1). A significantly higher proportion of immigrant boys and girls reported the use of vitamin D supplements compared with nonimmigrants. Among 1- to 2-y-old children, a significantly higher proportion of immigrant girls were breast-fed compared with nonimmigrant girls. Regarding the age group of 3–17 y, boys with an immigrant background had a significantly higher BMI, whereas immigrant girls had a significantly lower calcium intake index. In both sexes, immigrants had a significantly higher vitamin D intake index, a significantly larger media consumption, and significantly less physical activity. Food groups contributing to the higher vitamin D intake among immigrants were fish, eggs, cream cheese, and pancakes (data not shown). Vitamin D concentrations were consistently lower among immigrants compared with nonimmigrants in both sexes, with the exception of 1-y-old participants (Fig. 1A,B). Overall, there was an age dependency in serum 25(OH)D concentrations, beginning with very high concentrations among younger age groups and declining sharply among older age groups. A small
increase in 25(OH)D concentrations occurred in 14- to 17-y-old participants, especially among girls. Among 1- to 2-y-old infants, the prevalence of vitamin D deficiency differed between immigrants and nonimmigrants (especially among girls), although to a lesser degree than among participants in older age groups (Table 2). Among 3- to 17-y-old participants, 29% of immigrant boys and 31% of immigrant girls had severe to moderate vitamin D deficiency [25(OH)D ,25 nmol/L] compared with 18% of nonimmigrant boys and 17% of nonimmigrant girls. In the same age group, 91.8% of immigrant boys and 93.6% of immigrant girls had 25(OH)D concentrations ,75 nmol/L compared with 86.6% of non-immigrant boys and nonimmigrant girls. Overall, differences between immigrants and nonimmigrants were significant, except for 1- to 2-y-old boys. Independent determinants of serum 25(OH)D concentrations among immigrants 3 y of age and older consistently included the season of examination, socioeconomic status, and vitamin D supplement use in both sexes (Table 3). Additionally, living in nonmetropolitan areas, BMI groups, and physical activity were independent determinants of serum 25(OH)D concentrations in boys, whereas age, sexual maturation, and degree of integration contributed to the model in girls. Boys whose mothers' native countries were Turkey or Arab- Islamic countries had an increased risk of having low 25(OH)D concentrations (odds ratio [OR] 2.3; [95% CI] 1.4–3.8 and OR 7.6; [95% CI] 3.0–19.1, respectively) compared with nonimmigrants,
independent of relevant covariates (Table 4). The same was true for girls with a Turkish (OR 5.2; [95% CI] 2.9–9.6), Arab-Islamic (OR 5.9; [95% CI] 2.5–14.0), Asian (OR 6.7; [95% CI] 2.2–19.8), or African (OR 7.8; [95% CI] 1.5–40.8) background.

Discussion

We observed a high prevalence of vitamin D-deficient states among children and adolescents, especially among those beyond infancy. Notably high 25(OH)D concentrations were seen in 1-y-old children regardless of immigrant background. Most likely this is attributable to the recommended vitamin D supplementation during infancy in Germany. Regarding 1- to 2-y-old participants, nearly 30% of immigrant boys and 32% of immigrant girls took vitamin D supplements compared with 20% of nonimmigrant boys and 23% of nonimmigrant girls. The relatively higher proportion of supplement use among immigrants may be explained by pediatricians' increasing awareness of this problem. However, recommendations to supplement vitamin D during infancy were implemented ;50 y ago in Germany. We can therefore exclude that increased awareness results from recent changes in recommendations. Our study population did not include children ,1 y old, which would have probably increased the proportion of vitamin D supplement use. However, regarding all other ages (apart from 1-y-old participants), vitamin D concentrations were consistently lower among immigrants compared with nonimmigrants. Thus, despite a significantly higher proportion of vitamin D supplement users and higher vitamin D intake index, children with an immigrant background were significantly more likely to have inadequate vitamin D concentrations. The question whether vitamin D requirements are even higher among immigrants, especially those with a dark pigmented skin, should be discussed and the appropriate dosage of supplements needs to be

examined in intervention studies. Our results are consistent with those reported by Erkal et al. (5), who showed a high prevalence of vitamin D deficiency in Turkish immigrants aged 16 y and older living in Germany. Studies from other countries with similar findings have been previously conducted among immigrant children of Asian origin in the United Kingdom (33–35), among immigrant children of various origins in the Netherlands (17,36) and Denmark (37,38), as well as among African American children in the USA (39–42). Further studies demonstrated similar results in ethnic groups residing in New Zealand (16) or Canada (43). A comparison to published results on vitamin D status among children and adolescents of the presented age range (1–17 y) is difficult, because there has been no study so far, to our knowledge, including children across a comparably wide age range. To our knowledge, no previous European epidemiological study has investigated independent determinants of vitamin D status among immigrant boys and girls. There is a populationbased study examining determinants of hypovitaminosis D [as defined by 25(OH)D concentrations ,37.5 nmol/L] among African American women aged between 15 and 49 y (39). In contrast to our observations, hypovitaminosis D was associated with lower BMI in this group. In our study, being overweight (.90th–97th BMI percentile) and being obese (.97th BMI percentile) was negatively associated with serum 25(OH)D
concentrations in immigrant boys. These results are consistent with those of Reinehr et al. (44) showing that obese children had significantly lower 25(OH)D concentrations compared with nonobese children. In the German National Health Interview and Examination Survey 1998, we observed not only a high but also a low BMI associated with low serum 25(OH)D concentrations among adults (45). It is possible that growth in childhood and adolescence is responsible for the fact that the findings among children and adolescents are not consistent with those among adults. Furthermore, we assumed that body fat may be affecting the association between age and 25(OH)D levels, as it
may act as a reservoir for vitamin D. We therefore computed predicted body fat and replaced BMI with predicted body fat levels in multiple linear regression models with similar results; predicted body fat level was significantly and inversely related to serum 25(OH)D in boys as opposed to no association in girls. BMI or predicted body fat level did not explain the observed association between age and vitamin D status among girls. We did find a relationship between degree of integration and vitamin
D concentrations among girls. Including this variable into the models, it is likely to serve as a proxy variable for cultural/religious behavior (e.g. veiling) that was not captured by the constructs of
the defined countries of origins.
In the multivariate analyses, vitamin D intake index showed no association with 25(OH)D concentrations. We reran the model, using quintiles instead of tertiles of the vitamin D index with no change to the results. The influence of diet on vitamin D concentrations appears to be relatively small in comparison to UVradiation (46). To account for less UVexposure in the winter months, we also performed separate analyses for winter and summer (with no additional findings). It was our aim to identify groups at particularly high risk of vitamin D deficiency among immigrant children and adolescents. Turkish and Arab-Islamic participants of both sexes as well as Asian and African girls were found to be at high risk for vitamin D deficiency, with the highest OR for African girls (7.8).
Similarly, data from NHANES III showed that adolescents of African origin had an increased risk of vitamin D deficiency (OR 8.6) compared with white adolescents (47). It is likely that an increased pigmentation of the skin is partly responsible for these findings. The skin color characteristic is
mainly determined by the epidermal melanin content. Melanin absorbs UVradiation in competition with 7-dehydrocholesterol, which is the initial substrate for vitamin D production (48). Therefore, a higher level of skin pigmentation decreases the efficiency of the dermal synthesis of vitamin D (49–52). This
may, at least in part, explain why individuals with higher pigmented skin are particularly prone to vitamin D deficiency after immigrating to sun-deprived countries in higher latitudes. Among other aspects, the type of clothing determines the extent of sun exposure. Recent studies suggest that vitamin D deficiency is particularly common among young women who wear concealing
clothing (53–56) and who at the same time also have an increased risk of osteoporosis (57).
The association between Turkish background and 25(OH)D concentration , 25 nmol/L was even stronger among girls (OR 5.2) than boys (OR 2.3). This may be due to the common habit of veiling among Turkish girls in Germany. Because we had no information on participants' clothing habits, this remains only an assumption. However, this would not explain our findings that boys with Arab-Islamic background had an OR of 7.6 compared with girls (OR 5.9). Genetic factors may contribute to the
observed differences in vitamin D status according to ethnic background. There is evidence that plasma concentrations of calciotropic hormones, in particular circulating 25(OH)D, are under strong genetic control (58). Genetic variation in vitamin transport protein expression may play a role (59,60) and are likely to interact with environmental and behavioral factors. Epigenetic factors are also possible and may explain the previously observed association between skin pigmentation, vitamin
D deficiency, and the risk for several chronic diseases (61–63). In this study, we aimed specifically to examine vitamin D deficiency in association with an immigrant background among

children and adolescents in Germany. This was possible because the KiGGS survey included boys and girls with an immigrant background in numbers corresponding to their percentage of the population. Nevertheless, our results are subject to several study limitations. Because we had no information on the grade of skin pigmentation, we had to rely on information regarding the mothers' countries of origin. Countries were grouped with respect to geographical as well as cultural, religious, and lifestyle aspects. Information on diet was queried using a FFQ, which is regarded as being a relatively imprecise instrument. Furthermore, it was not developed with respect to obtaining specific information on foods containing vitamin D or calcium. The present analysis focused on serum 25(OH)D cut-points that maybe relevant to skeletal and extraskeletal health as suggested by current evidence from the biomedical literature. Evidence regarding the long-term outcomes of vitamin D deficiency and the benefits of vitamin D supplementation is still scarce due to the lack of long-term prospective and intervention studies. The relationship between serum concentrations of PTH and 25(OH)D may provide further insight; however, our data on serum PTH were available for only a small subset of study participants. Preliminary analyses suggest that no further suppression of PTH occurs beyond a 25-(OH)D concentration of 28 nmol/L. However, 25(OH)D thresholds varied according to age and immigrant background. Given the small number of observations within subgroups of children with an immigrant background and the fact that the association between serum PTH and 25(OH)D appears to be modified by multiple factors (64), it was beyond the scope of our study to investigate the relationship between serum PTH and serum 25(OH)D in more detail. In general, existing measurement methods are assumed to inadequately quantify 25-(OH)-ergocalciferol and particularly 25-(OH)-cholecalciferol and may, therefore, not capture serum levels derived from the use of vitamin D supplements containing only 25-(OH)-cholecalciferol. The chemiluminescence immunoassay has demonstrated better performance with respect to 25(OH)-ergocalciferol quantification than other assays (65) and thus was chosen for our study. Whereas vitamin D supplements in the US contain 25-(OH)-ergocalciferol, most vitamin D supplements in Germany contain 25-(OH)-cholecalciferol. Further analyses of information on vitamin D supplement use, derived from the CAPI, showed that the majority (approximately two-thirds) of children and adolescents took 12.5 mg 25- (OH)-cholecalciferol. Of those participants taking vitamin D supplements, .80% took them on a daily basis. In conclusion, we found a high prevalence of vitamin D deficiency among children and adolescents in Germany beyond infancy, which is even higher among those with an immigrant background despite a higher vitamin D intake index and a higher proportion of vitamin D supplement use. Immigrants with Turkish, Arab-Islamic, Asian, and African backgrounds are identified to be at particularly high risk. Vitamin D supplementation was a positive and significant determinant of vitamin D status in 3- to 17-y-old immigrant boys and girls. Therefore, extending vitamin D supplementation beyond infancy (especially in high risk groups) should be discussed. The appropriate dosage of supplements needs to be examined in intervention studies. Fortification of foods is a preventive measure and could be another option for improving vitamin D status. The effectiveness of preventive measures over time needs to be evaluated in appropriate studies.

Tables

TABLE 1: Participant characteristics (1-17 years and 3-17 years) by gender and immigrant background (in percent, %) [1]

Variable	non-immigrant boys (n=3,992)	immigrant boys (n=1,102)	non-immigrant girls (n=3,858)	immigrant girls (n=1,035)
	1-17 years		1-17 years	
Age group				
1-2 years	9.7	11.3	9.7	11.2
3-10 years	43.8	46.0	43.8	46.7
11-17 years	46.5	42.7	46.5	42.1 *
Season of examination (summer) [2]	49.8	47.7	46.9	46.9
Socio-economic status				
Low	22.4	44.5	21.8	44.7
Middle	47.9	38.0	47.9	36.6
High	29.7	17.5 ***	30.3	18.7 ***
Residence in East Germany	19.8	8.5 ***	19.4	8.5 **
Living in non-metropolitan areas	79.4	60.5 ***	80.8	60.0 ***
Breast feeding, among 1-2 years	4.0	6.4	3.8	12.8 *
Use of supplements				
Vitamin D	5.3	8.6 **	4.9	7.8 **
Calcium	7.5	8.2	6.1	7.1
Vitamin D, among 1-2 years	20.5	29.7	23.1	32.5
Vitamin D, among 3-17 years	3.6	5.7 **	3.0	4.5 *

Variable	non-immigrant boys (n=3,689)	immigrant boys (n=1,011)	non-immigrant girls (n=3,554)	immigrant girls (n=951)
	3-17 years		3-17 years	
BMI (kg/m^2) [3]				
< P3	2.3	1.3	1.7	1.5
P3-<P10	5.6	4.2	5.3	5.6
P10-P90	78.6	76.0	79.1	77.8
>P90-P97	8.1	10.5	7.9	9.1
>P97	5.4	8.0 ***	6.0	6.0
Sexual maturation [4]				
Tanner 1	49.7	52.2	49.1	52.2
Tanner 2-3	15.3	13.8	8.9	8.4
Tanner 4-6	35.0	33.9	42.0	39.4
Physical activity [5]				
Lower group	27.0	34.0	37.7	51.0
Middle group	36.1	34.3	34.2	27.5
Upper group	36.9	31.7 ***	28.1	21.5 ***
Media consumption [6]				
Lower group	30.2	19.5	44.9	32.4
Middle group	35.6	27.4	32.7	30.1
Upper group	34.2	53.1 ***	22.4	37.5 ***
Vitamin D intake index [7]				
Lower group	28.7	22.2	39.1	31.8
Middle group	33.9	31.8	34.6	31.7
Upper group	37.4	46.0 ***	26.3	36.5 ***
Calcium intake index [8]				

Lower group	30.5	33.6	35.4	42.4
Middle group	33.9	30.9	35.1	30.6
Upper group	35.6	35.5	29.5	27.0 **

[1] Data are percentages. Asterisks indicate a difference from non-immigrants of the same sex:
p<0.05=*, p<0.01=**, p<0.001=***
Variables are tested using chi square test statistic (adjusted F-value for the Wald log-linear chi square statistic).
[2] Winter (November – April), Summer (May - October).
[3] BMI was grouped according to age and sex specific BMI percentiles as proposed by Kromeyer-Hauschild (26): <3rd percentile (severely underweight), 3rd to 10th percentile (underweight), 10th-90th percentile (normal weight), 90th to 97th percentile (overweight), >97th percentile (obese).
[4] measured by Tanner stages with ranges from 1 to 6 according to Tanner.
[5] Age group 3-10 years: engagement in sports with or without a sports club: never or less than 1-2 times per week (lower group), 1-2 times per week (middle group), at least 3-5 times per week (upper group). Age group 11-17 years: being involved in sweat-inducing activities: never, seldom or at least 1-2 times per week (lower group), 3-5 times per week (middle group), almost every day (upper group).
[6] Age group 3-10 years: TV/Video or PC consumption: lowest tertile of summed hours per day (lower group), middle tertile of summed hours per day (middle group), highest tertile of summed hours per day (upper group).
Age group 11-17 years: TV/Video, PC or game console consumption: lowest tertile of summed hours per day (lower group), middle tertile of summed hours per day (middle group), highest tertile of summed hours per day (upper group).
[7] Vitamin D intake estimated using tertiles of the vitamin D intake index.
[8] Calcium intake estimated using tertiles of the calcium intake index.

TABLE 2: Prevalence of vitamin D deficient and replete states [2 3] by gender, age group and immigrant background (percentage and 95 % confidence limits, %) [1]

Variable	non-immigrant boys	immigrant boys	non-immigrant girls	immigrant girls	
1-2 years					
Severe vitamin D deficiency [2]	<12.5 nmol/L	0.5 (0.0-1.4)	1.3 (0.0-3.2)	1.3 (0.0-3.0)	2.3 (0.0-5.8)
Moderate vitamin D deficiency [2]	12.5-25 nmol/L	6.6 (3.5-9.7)	9.5 (3.4-15.6)	5.8 (2.4-9.0)	14.9 (5.7-24.1)
Mild vitamin D deficiency [2]	25-50 nmol/L	24.1 (18.3-29.9)	29.7 (19.6-39.8)	29.3 (22.3-36.3)	28.3 (18.8 37.8)
Replete vitamin D status [2]	50-75 nmol/L	31.0 (24.3-37.7)	24.9 (14.5-35.3)	33.9 (26.9-40.8)	14.3 (4.6-24.0)
Optimal vitamin D status [3]	>75 nmol/L	37.8 (30.6-45.0)	34.6 (22.1-47.0) n.s.	29.7 (23.0-36.5)	40.2 (29.4-51.0) *
3-17 years					
Severe vitamin D deficiency [2]	<12.5 nmol/L	3.0 (1.8-4.2)	6.9 (4.1-9.7)	2.5 (1.4.-3.5)	9.3 (6.5-12.1)
Moderate vitamin D deficiency [2]	12.5-25 nmol/L	14.7 (11.4-18.0)	21.9 (17.8-25.9)	14.3 (11.3-17.3)	21.9 (17.9-25.9)
Mild vitamin D deficiency [2]	25-50 nmol/L	44.1 (40.9-47.3)	47.1 (43.5-50.7)	46.6 (43.5-49.8)	45.4 (41.0-49.7)
Replete vitamin D status [2]	50-75 nmol/L	24.8 (21.6-28.0)	15.9 (12.8-19.0)	23.2 (20.1-26.3)	17.0 (13.2-20.7)
Optimal vitamin D status [3]	>75 nmol/L	13.4 (10.8-16.0)	8.2 (5.6-10.9) ***	13.4 (10.9-16.0)	6.4 (4.1-8.8) ***

[1] Variables are tested using chi square test statistic (adjusted F-value for the Wald log-linear chi square statistic), p<0.05=*, p<0.01=**, p<0.001***.
The sum of each column is 100%.
[2] Categories of serum 25(OH)D concentrations as described by Lips, 2004 (23).
[3] Cut-off point of serum 25(OH)D concentrations as described by Bischoff-Ferrari, 2006 (24).

TABLE 3 Independent determinants of serum 25(OH)D concentrations (immigrants 3-17 years): results of multiple linear regression models by gender

	Boys				Girls			
Parameter	Beta	SE	t-value	p-value	Beta	SE	t-value	p-value
Intercept	26.585	4.182	6.36	<0.001	15.129	4.481	3.38	0.001
Age	-0.604	0.389	-1.55	0.124	0.933	0.372	2.51	0.014
Season of examination (summer)	21.485	2.379	9.03	<0.001	18.842	2.209	8.53	<0.001
Socio economic status [reference=Low]								
Middle	4.753	2.065	2.30	0.023	1.394	2.220	0.63	0.531
High	6.378	3.260	1.96	0.053	8.856	3.292	2.69	0.008
Living in non-metropolitan areas	4.725	2.168	2.18	0.031	2.378	2.303	1.03	0.304
Use of vitamin D supplements	9.091	4.387	2.07	0.041	9.684	4.604	2.10	0.038
BMI (kg/m^2) [reference=P10-P90]								
< P3	-6.031	3.995	-1.51	0.134	9.408	10.633	0.88	0.378
P3-<P10	-4.843	4.142	-1.17	0.245	5.599	3.042	1.84	0.069
>P90-P97	-5.586	2.499	-2.23	0.028	-0.461	3.450	-0.13	0.894
>P97	-6.944	2.579	-2.69	0.008	2.430	3.259	0.75	0.457
Sexual maturation [reference=Tanner 1]								
Tanner 2-3	0.187	2.388	0.08	0.938	-7.906	2.328	-3.40	0.001
Tanner 4-6	1.611	3.556	0.45	0.652	-6.333	2.814	-2.25	0.027
Physical activity [reference=Lower group]								
Middle group	2.836	2.219	1.28	0.204	1.960	2.025	-0.97	0.335
Upper group	4.591	2.263	2.03	0.045	-2.410	1.995	-1.21	0.230
Degree of integration [reference=Low]								
Middle	1.320	2.812	0.47	0.640	0.521	3.038	0.17	0.864
High	3.098	3.007	1.03	0.305	8.649	2.101	4.12	<0.001
			R^2 = 0.2472					R^2 = 0.2398

TABLE 4 Relationship between vitamin D deficiency (serum 25(OH)D concentrations < 25 nmol/L) and mothers' country of origin (immigrants 3-17 years):

Odds Ratio (95% confidence limits) [1] [2] by gender

	Boys			Girls		
	n	OR (95 % CI) [1]	OR (95 % CI) [2]	n	OR (95 % CI) [1]	OR (95 % CI) [2]
Turkey	240	2.3 (1.5-3.3)	2.3 (1.4-3.8)	188	6.5 (4.6-9.4)	5.2 (2.9-9.6)
Eastern countries [3]	325	1.6 (1.1-2.1)	1.4 (0.9-2.1)	296	1.2 (0.8-1.8)	1.0 (0.6-1.5)
Southern Europe	153	1.6 (0.9-2.7)	1.0 (0.4-2.2)	170	2.1 (1.3-3.4)	1.6 (0.8-2.9)
Western countries [4]	121	1.1 (0.7-1.8)	0.8 (0.4-1.6)	129	0.7 (0.4-1.4)	0.8 (0.4-1.6)
Arab-Islamic countries	84	7.8 (4.3-14.3)	7.6 (3.0-19.1)	68	9.0 (4.8-16.9)	5.9 (2.5-14.0)
Latin-America	19	1.6 (0.4-5.9)	1.6 (0.3-8.9)	22	1.2 (0.3-4.5)	1.3 (0.3-5.9)
Asia	33	5.1 (2.0-13.1)	2.2 (0.4-11.8)	43	9.6 (3.9-23.8)	6.7 (2.2-19.8)
Africa	20	7.6 (1.5-39.8)	6.4 (0.6-64.1)	18	18.8 (6.3-56.7)	7.8 (1.5-40.8)
[Reference=non-immigrants (excluding immigrants from other countries)]						

[1] Values are adjusted for age and season of examination.

[2] Values are adjusted for age, season of examination, socio-economic status, residence in East Germany, living in non-metropolitan areas, use of vitamin D and calcium supplements, vitamin D and calcium intake index,
BMI groups, physical activity and media consumption.

[3] Central and Eastern Europe and former Soviet Republics.

[4] Western Europe, USA and C

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