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Abstract

Background: Vitamin D deficiency is a global health problem in children. The vitamin D status of children and adolescents has not been evaluated in Bahrain.

Aims: This cross-sectional study aimed to determine the prevalence of vitamin D deficiency in healthy children in Bahrain and investigate the relationship between vitamin D level and age and sex.

Methods: Medical records of children aged 1 month to 16 years who attended a vitamin D screening campaign at Al Kindi Specialized Hospital, Bahrain between September and October 2016 were reviewed. Data on sex and age were recorded and vitamin D level was measured as serum 25-hydroxyvitamin D [25(OH)D]. Children were grouped as: vitamin D sufficient [25(OH)D ≥ 75 nmol/L], vitamin D insufficient (51–74 nmol/L) and vitamin D deficient (≤ 50 nmol/L).

Results: A total of 531 children were included in the study, 50.8% of whom were boys. Most of the children (93.4%) had low vitamin D levels; 78.3% were vitamin D deficient and 15.1% vitamin D insufficient. Only 6.6% were vitamin D sufficient. A significantly greater proportion of girls were vitamin D deficient than boys (P < 0.01). More primary-school children and adolescents were vitamin D deficient than preschool children (P = 0.001). A negative correlation
was found between vitamin D level and age \( (r = -0.467; P < 0.0001) \). Regression analysis showed that vitamin D level decreased by \(-2.164 \text{ nmol/L}\) for each year of age.

Conclusion: Vitamin D deficiency is a problem among healthy children in Bahrain. Public health policies or interventions are suggested to improve vitamin D status in Bahrain, especially for school-aged children.

Keywords: vitamin D deficiency, child, adolescent, prevalence, Bahrain

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Introduction

Vitamin D is a vital steroid hormone (1). It is mainly produced in the skin after exposure to sunlight (1–3). If sun exposure is inadequate, vitamin D level can be maintained by taking supplements or foods that contain vitamin D (2). However, food sources of vitamin D are few (1,3).

Vitamin D has a crucial role in improving physiological function in both skeletal and extraskeletal tissues (1,2). It is essential for intestinal calcium absorption, homeostasis and bone mineralization, especially during infancy, childhood and puberty (1,2,4). Only 10–15% of dietary calcium is absorbed without vitamin D (1). Serum 25-hydroxyvitamin D \([25(\text{OH})\text{D}]\) levels less than 50 nmol/L can lead to a marked decrease in intestinal calcium absorption (1). This is associated with increased parathyroid hormone secretion and decreased insulin-like growth factor 1 (1). Serum 25(OH)D level is directly connected to bone mineral density with a maximum
density attained when the 25(OH)D level is ≥ 100 nmol/L (1). Severe vitamin D deficiency impairs bone mineralization leading to osteomalacia and rickets (2). Recent evidence shows that the role of vitamin D goes beyond calcium and phosphorous metabolism (3). Many extra skeletal illnesses have been associated with vitamin D deficiency, such as those related to fuel metabolism, the cardiovascular system, cancer and the immune system (1,3).

Despite several preventive approaches, vitamin D deficiency has remained a global health problem in children (2,3,5). Vitamin D status in children has been evaluated in many countries (1–11). In Bahrain, two published studies on vitamin D status looked at neonatal and adult age groups (12,13). To our knowledge, the vitamin D status of children and adolescents has not been evaluated in Bahrain.

This study aimed to determine the prevalence of vitamin D deficiency in a large sample of healthy children and adolescents in Bahrain, evaluate any sex and age differences between children with low vitamin D levels and those with adequate vitamin D, and correlate vitamin D levels with children’s age.

Methods

Study design and sample

This was a cross-sectional study in which the medical records of 593 healthy children who attended the vitamin D screening campaign at Al-Kindi Specialized Hospital, Bahrain between 27 September and 1 October 2016 were reviewed. The vitamin D screening campaign is a free campaign organized by Al-Kindi Specialized Hospital, a private hospital in Manama, the capital of Bahrain, as part of their social commitments to the community. This campaign is considered a national campaign as all healthy children in Bahrain were invited. The campaign was conducted in the clinics of the paediatrics department. Children were triaged by nursing staff before enrolment for blood collection. Children with any illness were excluded in this campaign. Children were also excluded from the study if they were under one month of age or more than 16 years, and data were missing on their health condition or serum 25(OH)D levels.

Data collection

Data on sex, age at attending the campaign and serum 25(OH)D level were collected. Age was divided into three groups: 1 month to 5 years (preschool), 6 to 10 years (school age) and 11 to 16 years (adolescent). Two millilitres of venous blood were collected from each child by trained nurses and kept in a plain tube as vitamin D test is dependent on the serum level so this type of tube should be used and not an ethylenediaminetetraacetic acid (EDTA) tube. The serum was separated from the whole blood and vitamin D levels were measured using an Elecsys vitamin D total assay (Roche Cobas E 411 analyser apparatus, Switzerland). Vitamin D status was
based on serum 25(OH)D level and categorized into three groups: vitamin D deficient [serum 25(OH)D ≤ 50 nmol/L], vitamin D insufficient (51–74 nmol/L) and vitamin D sufficient ≥ 75 nmol/L) (14,15).

### Statistical analysis

Data were analysed using SPSS, version 21. Frequencies and percentages for sex, age group and vitamin D group were calculated. Fisher exact and Pearson chi-squared tests were used to compare categorical variables (sex, age groups and vitamin D groups). Continuous variables (children’s age and vitamin D levels) were checked for normal distribution using the Kolmogorov–Smirnov test. Group data are presented as a mean and standard deviation (SD) or median and range. Vitamin D groups were compared using the Mann–Whitney U and Kruskal–Wallis tests. Spearman’s correlation coefficient (rs) was used to examine correlations between vitamin D level and the children’s age. Coefficient of determination (r2) and the simple regression equation were calculated. A P-value < 0.05 was considered statically significant.

### Ethical considerations

Informed consent was obtained from the parents before the blood test. Patients with vitamin D deficiency were offered a free consultation with a paediatrician to discuss the result of the test and they were advised to be treated with the appropriate doses of vitamin D therapy. This study was approved by the secondary care medical research subcommittee of Al-Kindi Specialised Hospital, Bahrain, and was conducted in accordance with the principles of Helsinki Declaration.

### Results

A total of 593 healthy children were tested for serum 25(OH)D level. The children came only for vitamin D screening and they were not seeking any medical consultation. Sixty-two (10.4%) children were excluded because they had no laboratory results because their blood samples were inadequate. No sick patient came for the screening; therefore no children were excluded based on the health condition. Clinical characteristics and laboratory results of the remaining 531 children are shown in Table 1. Of the 531 children, 270 (50.8%) were boys. Most of the children (93.4%) had low vitamin D levels; only 6.6% had an adequate vitamin D level. Mean serum 25(OH)D level was significantly lower in girls [37.4 (SD 19.9) nmol/L] than boys [43.4 (SD 22.4) nmol/L] (P < 0.001). Mean vitamin D levels for preschool children, primary-school children and adolescents were 47.4 (SD 22.4) nmol/L, 37.4 (SD 17.47) nmol/L and 27.45 (SD 17.47) nmol/L respectively (P<0.001).

Table 2 shows the demographic characteristics of the children categorized according to vitamin D level (sufficient and low). A greater proportion of girls (94.3%) had low vitamin D compared with boys (92.6%), but this was not statistically significant (P = 0.487). The mean and
median ages of the children with low vitamin D were significantly higher than those of children with adequate vitamin D levels ($P < 0.001$). A significantly greater proportion of primary-school children and adolescents had low vitamin D than preschool children ($P = 0.015$). Only two infants were under one year (six months and eight months); one had vitamin D deficiency (40.7 nmol/L) and the other had insufficient vitamin D (64.4 nmol/L).

The association between vitamin D group (vitamin D sufficient, vitamin D insufficient and vitamin D deficient) and sex and age is shown in Table 3. Significantly more girls were vitamin D deficient than boys ($P < 0.001$). In addition, significantly greater proportions of primary-school children and adolescents were vitamin D deficient compared with preschool children ($P < 0.001$).

The Spearman correlation coefficient test showed a moderate but statistically significant negative correlation between vitamin D level and children’s age ($r = –0.467; P < 0.001$). The coefficient of determination ($r^2$) was $–0.934$ meaning that 93.4% of the variance in vitamin D level was explained by children’s age. A simple linear regression was calculated to predict children’s vitamin D levels as an outcome variable based on their age as the predictor variable (Figure 1). A significant regression equation was found: $F(1,529) = 96.660; P < 0.001; R^2 = 0.154$. Children’s predicted vitamin D level is equal to $–2.164(Age)\text{ nmol/L} + 21.592$, when age is measured in years. Children’s average vitamin D level decreased by $–2.164$ nmol/L for each year of age.

**Discussion**

Our study showed a very high prevalence (93.4%) of low vitamin D levels in healthy children in Bahrain. Prevalence of vitamin D deficiency in neighbouring countries and worldwide is shown in Table 4 (1,3–10,12,13,16–21). The available evidence suggests that vitamin D deficiency is an important child health problem worldwide (1–13,16–21). Studies on vitamin D deficiency in child and adult populations across Europe show an overall prevalence of 13% (7260/55 844) (22). In a large, population-based Dutch cohort, 30% (1250/4167) of the children were deficient in vitamin D ($< 50$ nmol/L) and 66% (2750/4167) had insufficient vitamin D ($< 75$ nmol/L) (9). A study in the United States of America (USA) showed a higher prevalence of vitamin D deficiency of 40% (146/365) in healthy infants and toddlers (21). The first national estimate of rickets caused by vitamin D deficiency in Australia gave an incidence of 4.9/100 000 population a year in children ≤ 15 years (5).

Rickets caused by vitamin D deficiency has almost been eradicated in Western Europe and North America (1,23). However, the prevalence of vitamin D deficiency and rickets remains
unacceptably high in Asia, Africa and the Middle East (1). Compared with neighbouring countries, our study showed an almost similar prevalence of vitamin D deficiency in children (78.3%) as that reported in Oman (69.1%) (217/314), Kuwait (77%) (158/204) and Qatar (68.8%) (315/458) (16–18). However, the prevalence of vitamin D deficiency in our study was higher than that reported in Saudi Arabia (45.5%, 960/2110) (1). Similar to our study, a study from Fars Province, southern Islamic Republic of Iran, reported a very high prevalence of vitamin D deficiency of 81% (388/477) in children aged 9 to 18 years (7). A Korean study of children aged 6 to 12 years found that 59% (195/330) had vitamin D deficiency (6) and a study in Turkey found a prevalence of 40% (176/440) of poor vitamin D status among Turkish children aged 0–16 years (8).

As well as our high prevalence of vitamin D deficiency, 15.1% of the children and adolescents in our study had insufficient vitamin D (serum 25(OH)D = 52.4–72.4 nmol/L). Similarly, vitamin D deficiency ranged between 23% (49/209) at the end of summer and 80% (225/280) at the end of winter and vitamin D insufficiency between 12% (33/280) at the end of winter and 28% (58/209) at the end of summer in children in Ankara, Turkey (4). In a large cross-sectional study in Wuxi (southern China) among 5571 young children aged 1 to 3 years, vitamin D deficiency (serum 25(OH)D < 50 nmol/L) was found in only 897 (16%) (19). However, the number increased to 3058 (55%) when a higher cut-off for sufficient vitamin D level was considered (≥ 75 nmol/L) (19). Another study in China on 6008 children aged 1 month to 16 years showed a lower prevalence of vitamin D deficiency compared with vitamin D insufficiency (20). In Saudi Arabia, vitamin D deficiency and insufficiency were almost equal in children and adolescents between 6 and 15 years of age, 45.5% (960/2110) and 49.9% (1053/2110) respectively (1).

In our study, we focused on the role of sex and age of healthy children on the development of vitamin D deficiency. However, other factors can play a role in the increase of vitamin D deficiency, such as low vitamin D intake and low sunshine exposure (2,4,7,8,11). Moreover, breastfeeding, skin pigmentation, covering the skin, ethnicity, season, low physical activity and high fat mass index can lead to low vitamin D levels (2,7–9,16).

Although Bahrain is not affected by long winters, factors such indoor lifestyle, avoidance of exposure to sunlight, environmental pollution and the scarce dietary sources of vitamin D should be considered in relation to the high levels of vitamin D deficiency we found (3). However, an American study in 2008 found that skin pigmentation, sun exposure, time spent outdoors and sunscreen use were not predictors of 25(OH)D concentration or vitamin D deficiency, as was hypothesized (21). However, a recent study published in 2015 from the Islamic Republic of Iran showed that vitamin D concentration was associated with sun exposure, physical activity, age and pubertal status (7). Moreover, darker skin, limited sun exposure, less time spent outdoors, low physical activity and low dietary sources of vitamin D were also shown to reduce vitamin D concentration in other studies (2,9,18).
In our study, no significant differences were found between boys and girls in the overall occurrence of low vitamin D. However, a significantly greater proportion of girls were in the vitamin D deficiency group, and the mean serum vitamin D level was significantly lower in girls than boys. In China, no significant difference was found between males and females in vitamin D levels even though females had lower mean levels (47.92, SD 16.47 nmol/L) compared with males (53.4, SD 16.97 nmol/L) (20). In contrast, the Saudi Arabian study reported a significantly higher prevalence of vitamin D deficiency in 97.8% (1073/1097) of females compared with 92.8% (940/101) of males (P < 0.001) (1). This finding may be due to less sun exposure of females because of limited outdoor activities, conservative clothing and the use of sunscreen products for cosmetic reasons (1). Similarly, the study in Turkey found that vitamin D deficiency was higher in females at the end of summer (4). However, no significant relationship was found between sex and vitamin D level at the end of winter (4).

Our work showed a negative correlation between vitamin D level and children’s age. Similarly, the Iranian study showed that children’s age was inversely associated with vitamin D concentration even after adjustment for physical activity, puberty stage, sun exposure and fat mass index (7). The Turkish study also reported a negative correlation between age and vitamin D levels (4); the frequency of vitamin D deficiency increased with age and was highest in adolescents and older age groups (4). We found that a significantly greater proportion of primary-school children and adolescents were in the overall low vitamin D group and vitamin D deficiency group than preschool children. This finding is similar to studies in China, the Netherlands and Turkey (8,9,20). In Europe, vitamin D levels varied considerably depending on age group (22). On the other hand, studies in Korea, Unite Arab Emirates and the USA found no significant difference in age between children with vitamin D deficiency and those with vitamin D insufficiency (6,11,21). Further work is still needed to clarify if the vitamin D levels are really affected by children’s age. If this is the case, more studies are required to investigate the reasons for the decline in vitamin D levels in older children.

All the participants in our study were apparently healthy children. Children’s vitamin D status is not typically assessed as part of routine care (21). In fact, most people with vitamin D deficiency are asymptomatic or may present with vague and non-specific symptoms (1,21). These symptoms include muscle cramps, pain in weight-bearing joints, difficulty in walking, facial twitches and carpopedal spasms and may go unobserved for a long time (1,4). During childhood, clinical symptoms of vitamin D deficiency include hypocalcaemic seizures, lower-limb deformities, fractures, abnormal dentition and delayed developmental milestones (2). If vitamin D deficiency is severe and/or prolonged, linear growth impairment and many skeletal disorders may develop (1). However, obvious rickets and osteomalacia are only the tip of the iceberg in patients with severe vitamin D deficiency (1). Vitamin D deficiency has been shown to be associated with diseases related to: insulin production such as diabetes mellitus, hypertension, cancer and the immune system (3,15,16). Even active rickets may not be identified on physical
examination (4).

Most of the studies we reviewed used serum 25(OH)D level as a measure of vitamin D status in children (1,3–13,16–22) as we did. However, the cut-off points to decide vitamin D insufficiency and vitamin D deficiency are variable. Unlike our study where vitamin D levels of 50–74 nmol/L and ≤ 50 nmol/L were considered as vitamin D insufficiency and vitamin D deficiency respectively, the American Pediatric Endocrine Association recommends levels of 37.4–50 nmol/L as vitamin D insufficiency and < 37.4 nmol/L as vitamin D deficiency (24). It is important to use standardized serum 25(OH)D data in the assessment of the prevalence of vitamin D deficiency (20). In the Chinese study in Hangzhou, if the vitamin D deficiency threshold was changed to < 75 nmol/L, almost all children had low vitamin D levels (20). There is generally agreed that no individuals in the population should have a 25(OH)D concentration < 25–30 nmol/L (22). In Europe, after standardization of serum 25(OH)D data, the prevalence vitamin D deficiency was revised upwards and downwards in some studies (22). However, standardization has very little effect on 25(OH)D data if the population samples are small (22).

Our study has some limitations. The prevalence of vitamin D deficiency was determined using a sample of children presenting to one hospital so the results may not be representative of the whole population of Bahrain. A nationwide study would give a more accurate reflection of the true prevalence. Another limitation is that other factors affecting vitamin D levels were not reviewed, such as sun exposure, indoor life style, clothing, dietary intake of vitamin D, seasonal variation and environmental pollution.

Despite the limitations, our study is the first attempt to investigate vitamin D status among children aged 1 month to 16 years in Bahrain. The key strength was the inclusion of large number of healthy children with a wide range of ages. Our results suggest that paediatricians should have a higher degree of clinical suspicion for vitamin D deficiency and should screen all children with non-specific musculoskeletal pain. Moreover, the study provides further evidence to support public health policies or interventions to improve vitamin D status in Bahrain, especially for school-aged children as a targeted population.

**Conclusion**

Vitamin D deficiency is a very common problem among healthy children aged 1 to 16 years in Bahrain. Girls were more affected than boys and age was negatively correlated with vitamin D level. Further studies are needed: to calculate the prevalence of vitamin D deficiency in children sampled on a population basis; to evaluate the relationship between vitamin D level and other risk factors; to determine whether vitamin D deficiency during childhood affects later health; and to recommend preventive and therapeutic practices to avoid the long-term complications of
such a hidden medical problem.

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References


