The natural history of vitamin D deficiency in African refugees living in Sydney

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ABSTRACT

Objective: To describe the natural history of vitamin D deficiency in an at-risk population of African migrants living in Sydney.

Design, setting and participants: Opportunistic study of 25-hydroxyvitamin D [25(OH)D] concentrations over time in a community-based cohort of North African refugee families living in south-western Sydney. As part of a health-screening program, serum concentrations of 25(OH)D, parathyroid hormone (PTH), calcium, phosphate (PO_4) and alkaline phosphatase (ALP) were measured in September 2006 (end of winter, T1). Results for 25(OH)D were made available, and treatment was recommended as appropriate. In February–March 2007 (end of summer, T2), in the setting of a separate study of high-dose vitamin D (stoss) therapy, the same cohort was contacted, and measurements were repeated.

Main outcome measures: Changes in 25(OH)D, PTH, ALP and PO_4 concentrations between T1 and T2 in those who had not received vitamin D supplementation in the intervening period.

Results: We collected data from 149 participants at T1; by T2, 58 participants (39%) had been excluded or lost to follow-up. Data from 91 participants (46% female), all of whom had Type VI (very dark) skin pigmentation, were included in the analysis. All 91 were 25(OH)D deficient at T1. Between T1 and T2, mean 25(OH)D serum concentration increased from 19 nmol/L (SD, 5.6 nmol/L) to 36 nmol/L (SD, 12.4 nmol/L) ($P < 0.001$). Of the 91 participants, 79 (87%) remained vitamin D deficient at T2. Serum PTH and ALP activity decreased between T1 and T2 ($P < 0.05$).

Conclusion: Despite a significant increase in 25(OH)D serum concentration over the study period, most participants (87%) remained 25(OH)D deficient at the end of summer. Our results support the current consensus that recommends annual screening for vitamin D deficiency and routine vitamin D supplementation in at-risk populations, such as dark-skinned or veiled groups.

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Despite being readily preventable and treatable, simple vitamin D deficiency-related rickets and osteomalacia have made a global resurgence.[1-8] Known risk factors for vitamin D deficiency include dark skin pigmentation, cultural practices such as veiling and covering, insufficient exposure to sunlight, and exclusive breastfeeding beyond 6–12 months for at-risk groups.[5,9,10]

Although simple vitamin D deficiency is often asymptomatic, adults may present with bone pain, myalgia, myopathy, increased risk of falls, osteoporosis and hip fractures.[5,6,11,12] Infants with vitamin D deficiency usually have mothers who are also vitamin D deficient.[13,14] Children may present with hypocalcaemic seizures, rickets, bowed limbs, fractures and motor delay.[5,7] Furthermore, vitamin D is not only a calciotropic hormone, it may also have an important role in cell growth and immunomodulatory effects.[15-19]

In Australia, most vitamin D is obtained through exposure to ultraviolet B (UVB) radiation in sunlight. There are adult exposure recommendations to prevent vitamin D deficiency, but because 95% of skin cancers and 99% of melanomas in Australia are due to sun exposure, it is difficult to make similar recommendations for children.[20-22] Further, as skin pigmentation increases, so too does the period of exposure to UVB required to synthesise adequate amounts of vitamin D.[23]

Seasonal variation in 25-hydroxyvitamin D [25(OH)D] serum concentrations has been described previously in cross-sectional studies.[2,8,24,25] However, data on the natural history of vitamin D deficiency in at-risk populations are lacking.

Here, we describe the vitamin D concentrations at the end of winter and end of summer in a cohort of community-dwelling African refugees living in Sydney, New South Wales, and examine whether seasonal differences exist. We also explore differences between subgroups based on age, sex and dwelling type.

METHODS

Setting and population

Serum 25(OH)D concentrations were measured in a population of North African refugee families living in south-western Sydney, who had migrated to Australia before 2005. The first 25(OH)D measurement was done as part of a pilot health-screening program. The second measurement was collected at the beginning of a separate study of high-dose vitamin D (stoss) therapy for vitamin D deficiency. As such, this is an opportunistic report of vitamin D concentrations in the same population at two time points.

Data collection

As part of the screening program, serum concentrations of 25(OH)D, calcium, phosphate (PO_4), alkaline phosphatase and parathyroid hormone were measured. These serum samples were taken at the end of winter, in September 2006 (T1).

Calcium, PO_4 and alkaline phosphatase concentrations were measured using the VITROS 5,1 FS Chemistry System (Ortho Clinical Diagnostics, Rochester, NY, USA). Radioimmunoassays (Immunodiagnostic Systems, Boldon, UK) were used to measure 25(OH)D concentration, and parathyroid hormone concentration was assessed by immunometric assay (IMMULITE 2000, Siemens, Los Angeles, Calif, USA).

At the end of summer in 2007, a trial of high-dose vitamin D for the treatment of vitamin D deficiency became available, and we contacted the cohort from T1 about participation in this trial. Before enrolment, serum concentrations of 25(OH)D and other variants were measured again, in February–March 2007 (T2). Participants who were still deficient were given standard vitamin D therapy or, if eligible, enrolled in the trial. Only data from participants who had not received vitamin D supplementation between T1 and T2 were included in our analyses.

Change in vitamin D concentrations and variables related to bone and mineral metabolism between winter (T1) and summer (T2) in 91 African migrants living in Sydney

	Total no. (no. of females)	Serum concentration (SD)		*P*
		T1	T2	(T1 v T2)
25(OH)D (nmol/L), by age				
1–5 years	12 (4)	19 (10.8)	43 (13.2)	0.002
6–10 years	25 (8)	17 (5.2)	37 (11.2)	< 0.001
11–15 years	17 (9)	17 (4.4)	35 (10.3)	0.001
⩾ 16 years	37 (21)	21 (6.1)	34 (13.4)	< 0.001
Overall	91 (42)	19 (5.6)	36 (12.4)	< 0.001
Parathyroid hormone (pmol/L)*	—	6.9 (7.6)	3.8 (2.4)	< 0.001
Alkaline phosphatase (IU/L)†	—	225 (141)	210 (126)	0.03
Phosphate (mmol/L)‡	—	1.46 (0.29)	1.49 (0.30)	0.20
Calcium (mmol/L)§	—	2.35 (0.09)	2.34 (0.08)	0.20

25(OH)D = 25-hydroxyvitamin D. * Reference range (RR) = 1.0–7.0 pmol/L. † RR = 30–391 IU/L. ‡ RR = 0.81–2.20 mmol/L. § RR = 2.10–2.74 mmol/L. ◆

Demographic data, including date of birth, sex, country of origin and type of skin pigmentation, were recorded. Vitamin D deficiency and severity of the deficiency were defined as previously described:[9] serum concentrations of 25(OH)D ⩾ 50 nmol/L were regarded as sufficient; and concentrations of ⩾ 25 to < 50 nmolL, ⩾ 12.5 to < 25 nmol/L, and < 12.5 nmol/L were classified as mild, moderate and severe deficiency, respectively. Dwelling type was determined from the address as either a freestanding house or an apartment.

Statistical analyses

We used SPSS, version 15.0 (SPSS Inc, Chicago, Ill, USA) for statistical analyses. Differences between the groups completing follow-up at T2 and those with a single visit were evaluated with the Mann–Whitney rank test. We used paired *t* tests to analyse differences in normally distributed variables between T1 and T2, and the Wilcoxon signed rank test for non-parametric variables. Differences between types of dwelling at T1 and T2 were evaluated with independent *t* tests. We used two-way analysis of variance (ANOVA) to evaluate the difference in serum 25(OH)D between T1 and T2 with respect to age and sex.

The stoss therapy trial was approved by the ethics committee of the Children's Hospital at Westmead, Sydney, while the initial screening program was approved by the ethics committee of Sydney West Area Health Service. We obtained verbal consent from participants through health care interpreters.

RESULTS

Between 8 August 2006 and 25 September 2006, 149 people took part in the screening program and provided T1 serum samples. Mean 25(OH)D concentration was 20.4 nmol/L (SD, 9.3 nmol/L); vitamin D deficiency was mild in 23 attendees (15%), moderate in 113 (76%), and severe in 11 (7%), while 2 (1%) were 25(OH)D sufficient.

The 11 participants with severe vitamin D deficiency, and another with hypocalcaemia, paraesthesiae and muscle spasms, were immediately referred to hospital for review and management. All other participants were informed of their results, and letters sent to their family doctors with results and treatment recommendations.

Fifty-eight people (39%) who gave a serum sample at T1 did not attend follow-up at T2: five had moved interstate, 10 had received vitamin D supplementation, seven had enrolled in a vitamin D therapy trial, and 36 were lost to follow-up. In this group, 31 were female (53%), median age was 12.7 years (range, 2–62 years), and mean 25(OH)D concentration at T1 was 23 nmol/L (SD, 13.0 nmol/L).

Of the remaining 91 participants who provided serum samples at T2, all had been 25(OH)D deficient at baseline: deficiency was mild in 11 (12%), moderate in 71 (78%) and severe in nine (10%). Forty-two of these 91 participants were female (46%) and baseline median age was 11.5 years (range, 3–62 years). Eighty per cent were from Sudan, 17% from Egypt and 3% from Kenya, and all had Type VI (very dark) skin pigmentation.

Mean 25(OH)D concentration was 19 nmol/L (SD, 5.6 nmol/L) at T1 and 36 nmol/L (SD, 12.4 nmol/L) at T2 ($P < 0.001$) (Box). Seventy-nine participants (87%) were vitamin D deficient at T2; deficiency was moderate in 11 (12%), and mild in 68 (75%). There were no significant baseline differences in 25(OH)D concentration ($P = 0.08$), age ($P = 0.54$) or sex between the group included in analyses and those who did not complete follow-up.

The smallest increase in serum 25(OH)D concentrations between T1 and T2 was in participants aged 16 years or older ($P = 0.003$; ⩾ 16 years versus 15 years and younger) and in females ($P = 0.049$; females [T1] versus females [T2]). At T2, men and boys had a higher 25(OH)D concentration (40 nmol/L ± 13.9) than female participants (33 nmol/L ± 8.9) ($P = 0.008$); this difference was not apparent at T1.

Overall, there were significant decreases in serum concentrations of parathyroid hormone ($P < 0.001$) and alkaline phosphatase ($P = 0.03$) between T1 and T2, but serum calcium and PO_4 levels remained stable. Dwelling type had no influence on vitamin D levels (data not shown).

All participants were eucalcaemic throughout the study, and there were no adverse events.

DISCUSSION

These longitudinal data describe the seasonal variation of serum 25(OH)D concentrations in an African refugee population living in Australia. Simple vitamin D deficiency was universal in our cohort at the end of winter, and 87% of participants remained deficient at the end of summer. Corresponding decreases in parathyroid hormone and alkaline phosphatase concentrations suggest that, although asymptomatic, 25(OH)D deficiency had a metabolic effect on bone.

Adherence to recommended vitamin D therapy was poor following T1, even in those referred directly to hospital. This has been our previous experience in refugee populations, and was the impetus for developing a study into the usefulness of stoss vitamin D therapy.

The long-term effects of chronic childhood simple vitamin D deficiency in paediatric and adult bone disease are not well understood. However, there is mounting evidence to support the theory that optimal health requires much higher serum concentrations of 25(OH)D than those needed to prevent clinical signs of deficiency.[12,15,24,26]

Of particular concern is our finding that the smallest improvements in serum 25(OH)D over time were in women and participants aged 16 years or older. Infants born to vitamin D-deficient women will inherit this problem, thus perpetuating a cycle of vitamin D deficiency.[5,14,27,28] Maternal vitamin D deficiency is associated with decreased bone accrual in children[28,29] and may increase the risk of fragility fractures in adult life.[24,30]

Limitations of this study include the high rate of drop-out and a lack of data on intake of calcium and vitamin D dietary intake. Nonetheless, our data support the current recommendations for the prevention and treatment of simple vitamin D deficiency in Australian children and adults.[9,10]

These recommendations suggest:

- annual measurement of 25(OH)D in dark-skinned or veiled infants, children and adults;
- screening for simple vitamin D deficiency in the first trimester of pregnancy for dark-skinned or veiled women;
- vitamin D supplementation (400 IU daily) in breastfed infants of dark-skinned or veiled women until 12 months of age; and
- preventive daily 400 IU vitamin D supplementation in at-risk groups.

COMPETING INTERESTS

None identified.

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