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Case Report

Vitamin D status in children over three decades — Do children get enough vitamin D?

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ABSTRACT

Vitamin D is a key player in the endocrine regulation of calcium and phosphate metabolism and plays a pivotal role in the acquisition of bone mass during childhood. This study investigated long-term data of vitamin D levels in children and adolescents between 1 and 18 years of age. Serum 25-hydroxyvitamin D (25(OH)D) was analyzed between 1982 and 2013 in 2048 Swedish Caucasian children (mean age ± SD, 8.59 ± 3.68 years; 1197 boys). Overall, 704 (34%) children had below recommended levels of 50 nmol/L; however, only 63 (3%) had levels below 25 nmol/L, i.e., vitamin D deficiency. No trend for decreased vitamin D levels over time was found in this population, with median 25(OH)D levels of 58.4 nmol/L, minimum–maximum 5.0–159.3 nmol/L. Younger children, independent of gender, had significantly higher levels 25(OH)D.

The importance of vitamin D for skeletal health is well established and its potential role in extraskeletal health has generated much interest in recent years. A recent umbrella review summarized that vitamin D deficiency is linked to an array of chronic diseases, e.g., diabetes, autoimmunity, cancer, and is associated with negative cardiovascular outcomes (Theodoratou et al., 2014). Data from a large study demonstrated a J-shaped association of all-cause mortality with serum 25-hydroxyvitamin D (25(OH)D), and the lowest mortality risk was at 50–60 nmol/L (Durup et al., 2012). Vitamin D status is defined by serum 25(OH)D, and a concentration of 50 nmol/L (20 ng/mL) cover the requirements in 97.5% of the population (Ross et al., 2011). Solar UV-B radiation is important for endogenous vitamin D synthesis; however, sunlight is limited at the latitude 55–69 during October to March,(van Schoor & Lips, 2011) but Swedish children generally have a high intake of vitamin D from dietary products.

We hypothesized that the generally increased indoor activities would contribute to decreased vitamin D levels in children over the years. The present study provided long-term data of vitamin D levels in a group of children between 1 and 18 years of age referred over 30 years for extensive growth evaluation to Göteborg Pediatric Growth Research Center (GP-GRC), who were diagnosed with short stature due either to idiopathic or organic cause of growth hormone (GH) insufficiency, to decreased GH responsiveness as in children with idiopathic short stature, born small for gestational age or children with syndromes or chronic diseases; and also healthy children with normal or tall stature.

Serum 25(OH)D was analysed between 1982 and 2013 in 2048 Swedish Caucasian children (mean age ± SD, 8.59 ± 3.68 years; 1197 boys) with the IDS-iSYS 25-Hydroxy Vitamin DS automated chemiluminescence immunoassay (Immunodiagnostic Systems Limited, Boldon, UK) at the GP-GRC laboratory (Swedac accredited no. 1899). The intra-assay and interassay coefficients of variation were 2.5% at 50.1 nmol/L and 9.0% at 55.0 nmol/L, respectively. All samples in the present study were stored at −80 °C and assayed with reagents from the same batch in days after each other. In general, serum 25(OH)D is regarded as a stable analyte over time (Bailey et al., 2013; Stepman et al., 2011), and studies of 40-year-old sera have revealed that 25(OH)D can be quantified to reveal potential trends that can be used to explore vitamin D-related hypotheses (Bodnar et al., 2009). Taken together, we conclude that our 25(OH)D levels, sampled over a 30-year period, are reliable even if the possibility exists that the 25(OH)D levels could change during long-term storage never can be ruled out.

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Table 1
Yearly average values of 25(OH)D from 1982 to 2013.

	25(OH)D (nmol/L)		
Year	Median	Min	Max
1982	75.0	61.8	88.1
1983	53.2	39.5	99.2
1984	62.2	27.6	108.4
1985	58.4	24.7	103.9
1986	50.8	28.0	122.8
1987	47.9	14.5	113.1
1988	54.2	18.4	115.4
1989	56.6	13.5	111.8
1990	53.7	23.5	134.8
1991	67.3	19.3	130.8
1992	59.2	12.6	149.2
1993	52.4	21.1	129.4
1994	58.6	15.3	111.5
1995	46.8	13.8	136.5
1996	52.5	18.5	103.0
1997	61.4	13.0	145.1
1998	53.8	15.6	108.6
1999	52.3	15.9	106.5
2000	57.4	19.6	103.1
2001	56.1	12.9	113.5
2002	71.9	20.2	120.0
2003	71.4	24.6	159.3
2004	68.0	16.6	138.2
2005	59.7	13.0	133.7
2006	62.3	25.0	109.4
2007	65.0	21.8	119.6
2008	72.8	29.9	128.1
2009	78.6	38.5	107.6
2010	62.0	14.1	87.1
2011	63.3	5.0	103.1
2012	61.4	23.8	119.0
2013	48.4	26.9	63.9

The yearly average values of 25(OH)D from 1982 to 2013 are presented in Table 1. No trend for decreased vitamin D levels over time was found, with median 25(OH)D levels of 58.4 nmol/L, minimum–maximum 5.0–159.3 nmol/L (Fig. 1, upper panel). We found a significant association ($p < 0.00001$) with age independent of gender, i.e., younger children had higher 25(OH)D levels, possibly due to the general supplementation of vitamin D recommended for Swedish infants (Fig. 1, lower panel). To analyze a possible general trend in 25(OH)D, linear regression was performed to represent the moving average over the 30 years. The monthly averages for 25(OH)D were calculated from March 1982 to January 2013 ($n = 325$). A linear regression model was fitted to the data with the dependent variable being monthly average of 25(OH)D adjusted for age under 5 years and the independent variable being time. No trend for 25(OH)D was found ($r^2 = 0.0352$, p-value = 0.7507).

Overall, 704 (34%) children had below recommended levels of 50 nmol/L, and 63 (3%) had levels below 25 nmol/L, i.e., vitamin D deficiency (Ross et al., 2011). Less attention has been given to recommend an upper limit of serum 25(OH)D; however 83 (4%) subjects had 25(OH)D levels above 100 nmol/L of whom 15 (1%) had levels above 125 nmol/L (Ross et al., 2011).

The presence of 3-epi-25(OH)D, a vitamin D metabolite with reported reduced biological activity, has been reported to be a source of analytical variance in immunoassays (Bailey et al., 2013). In addition, an age-dependent concentration has also been reported (Stepman et al., 2011). The cross-reactivity for 3-epi-25(OH)D is approximately 1% in the automated IDS-iSYS immunoassay used in the current study. Thus, due to the low cross-reactivity, we do not believe that potential amounts of 3-epi-25(OH)D overestimates the reported 25(OH)D values in this study.

In conclusion, we found no trend for decreased vitamin D levels over time in this Swedish population. These results will broaden our understanding of the public health relevance of vitamin D and be of value for future cost–benefit analyses in preventive healthcare.

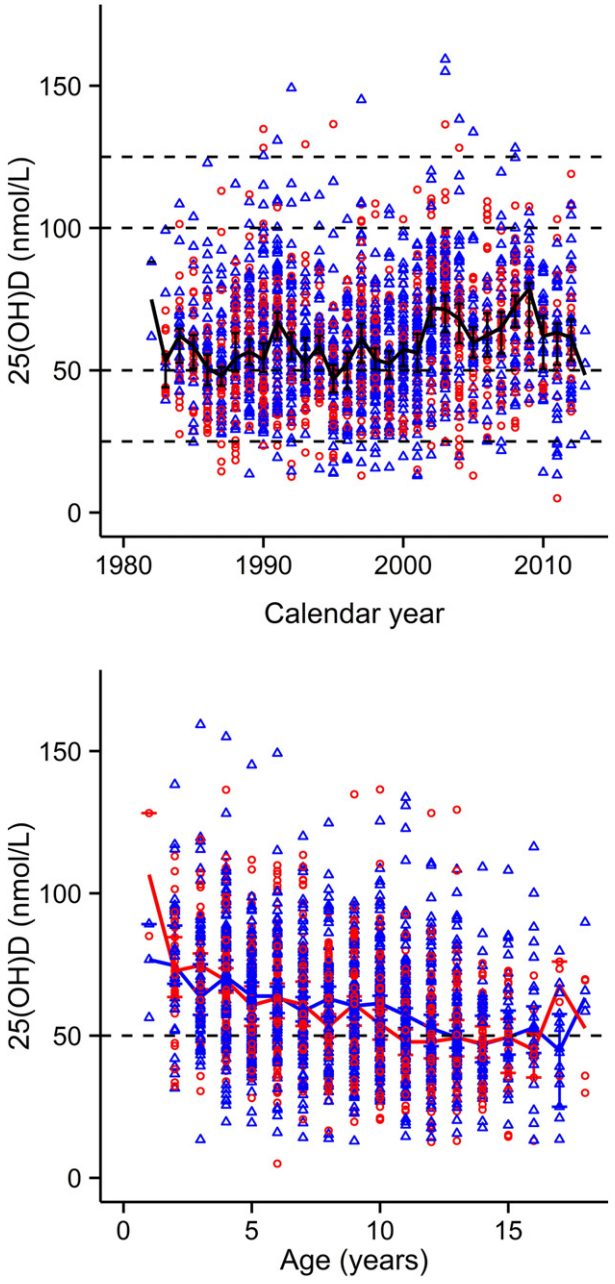

Fig. 1. Serum 25(OH)D levels in 2048 Swedish children over 32 years. Upper panel: Calendar years, 1982–2013, versus 25(OH)D levels. Median (black line) and 95% confidence intervals (for each year) are shown in 2048 Swedish children, 1197 boys (blue squares) and 851 girls (red circles). Black dotted horizontal lines represent 25(OH)D levels at 25, 50, 100 and 125 nmol/L. Above 125 nmol/L, n = 15 (1%); 100–125 nmol/L, n = 68 (3%); 75–99 nmol/L, n = 377 (18%); 50–74 nmol/L, 884 (43%), 25–49 nmol/L, n = 641 (31%); below 25 nmol/L, n = 63 (3%). Lower panel: Age versus 25(OH)D levels. Data represent median and 95% confidence intervals for 1197 boys (blue line; squares) and 851 girls (red line; circles). There was a significant decreasing trend with age independent of gender, $p < 0.00001$. Black dotted horizontal lines represent the recommended 25(OH)D level of 50 nmol/L.

Declaration of interests

We declare no competing interests.

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References

Bailey, D., Veljkovic, K., Yazdanpanah, M., Adeli, K., 2013. Analytical measurement and clinical relevance of vitamin D(3) C3-epimer. Clin. Biochem. 46, 190–196.

Bodnar, L.M., Catov, J.M., Wisner, K.L., Klebanoff, M.A., 2009. Racial and seasonal differences in 25-hydroxyvitamin D detected in maternal sera frozen for over 40 years. Br. J. Nutr. 101, 278–284.

Durup, D., Jorgensen, H.L., Christensen, J., Schwarz, P., Heegaard, A.M., Lind, B., 2012. A reverse J-shaped association of all-cause mortality with serum 25-hydroxyvitamin D in general practice: the CopD study. J. Clin. Endocrinol. Metab. 97, 2644–2652.

Ross, A.C., Manson, J.E., Abrams, S.A., Aloia, J.F., Brannon, P.M., Clinton, S.K., Durazo-Arvizu, R.A., Gallagher, J.C., Gallo, R.L., Jones, G., Kovacs, C.S., Mayne, S.T., Rosen, C.J., Shapses, S.A., 2011. The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. J. Clin. Endocrinol. Metab. 96, 53–58.

Stepman, H.C., Vanderroost, A., Stockl, D., Thienpont, L.M., 2011. Full-scan mass spectral evidence for 3-epi-25-hydroxyvitamin D(3) in serum of infants and adults. Clin. Chem. Lab. Med. 49, 253–256.

Theodoratou, E., Tzoulaki, I., Zgaga, L., Ioannidis, J.P., 2014. Vitamin D and multiple health outcomes: umbrella review of systematic reviews and meta-analyses of observational studies and randomised trials. BMJ 348, g2035.

van Schoor, N.M., Lips, P., 2011. Worldwide vitamin D status. Best Pract. Res. Clin. Endocrinol. Metab. 25, 671–680.