Postnatal evaluation of vitamin D and bone health in women who were vitamin D-deficient in pregnancy, and in their infants

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ABSTRACT

Objective: To determine the postnatal vitamin D status and bone health of women identified as vitamin D-deficient in pregnancy, and of their infants.

Design and participants: Retrospective audit conducted between 27 August and 5 November 2003. The study included women delivering between August and October 2002 at the Royal Women's Hospital, Melbourne, who had had a 25-hydroxyvitamin D (25-[OH]D) level < 30 nmol/L in pregnancy, and their infants at age 4–10 months.

Setting: The outpatient clinic at the Royal Children's Hospital, Melbourne.

Main outcome measures: Maternal and infant serum levels of vitamin D, total alkaline phosphatase (tALP), parathyroid hormone (PTH), calcium and phosphorus; x-ray results in children with clinical or laboratory findings suggestive of rickets.

Results: Of 69 mother–infant pairs invited to participate, 47 (68%) attended. All 47 women had 25-(OH)D levels < 50 nmol/L, and 39 (83%) had levels < 30 nmol/L. Vitamin D supplements had been prescribed in pregnancy for 35 women (74%), and 19/35 reported having taken them as prescribed. None had continued to take supplements postnatally, but one had recently started taking them again. Among 45 infants from whom blood samples were successfully obtained, 18 (40%) had 25-(OH)D levels < 50 nmol/L, and 14 (31%) had levels < 30 nmol/L. Twelve of 16 breastfed infants had 25-(OH)D levels < 30 nmol/L, compared with 2/29 fed formula milk ($P = 0.001$).

Conclusions: Most mothers who had been vitamin D-deficient in pregnancy were also deficient postnatally, indicating that treatment offered, counselling and/or treatment compliance were inadequate. Their infants, especially if breastfed, were at high risk of vitamin D deficiency and increased bone formation. Breastfed infants of mothers at high risk of vitamin D deficiency should receive vitamin D supplements.

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Vitamin D deficiency is re-emerging as a significant health problem among pregnant women and their infants,[1-6] particularly among groups with dark skin[1,4] or low skin exposure to sunlight.[7,8]

Vitamin D is a steroid hormone essential for calcium homoeostasis and maintenance of bone health. About 90% of our vitamin D comes from conversion of 7-dehydrocholesterol to cholecalciferol in skin exposed to ultraviolet B light.[9] Prolonged deficiency of vitamin D results in infantile rickets and adult osteomalacia.

The primary aim of our study was to determine the postnatal vitamin D status and bone health of women who had been identified as vitamin D-deficient in pregnancy, and of their infants.

METHODS

Our audit was approved by divisional directors of the Royal Women's Hospital and the Royal Children's Hospital in Melbourne as part of good clinical care.

Our study was conducted between 27 August 2003 and 5 November 2003. From computerised pathology records, we identified women delivering at the Royal Women's Hospital between August and October 2002 who had 25-hydroxyvitamin D (25-[OH]D) levels < 30 nmol/L during pregnancy. Their infants were aged 4–10 months at the time of the audit. Sixty-nine women were sent a letter (in English, with one reminder) inviting them to attend a dedicated outpatient clinic at the Royal Children's Hospital to have their own and their infant's vitamin D status and bone health assessed. Hospital interpreters were available.

Demographic and physical data

We recorded information on maternal vitamin D supplementation, age, country of birth, first language, religion, wearing of a hejab (headscarf), skin colour ("light" or "dark") and whether the women had access to an outdoor family area at home. In their infants, we investigated feeding, illnesses since birth, and supplementation with vitamin D. All infants were examined by M R Z or K T for evidence of rickets.

Biochemical tests

Verbal consent was obtained for venepuncture of both mother and baby. Serum levels of calcium, phosphate and total alkaline phosphatase (tALP, a surrogate measure of bone ALP and thus of bone formation) were measured by a Vitros 250 analyser (Ortho Clinical Diagnostics, Buckinghamshire, UK) using standard kit methods (normal range for tALP, < 120U/L [adults] and < 350 U/L [children 0–2 years]). Intact serum levels of parathyroid hormone (PTH) were measured by an Immulite 2000 analyser (Biomedic DPC, Melbourne, VIC) (normal range, 1.3–6.8 pmol/L for infants and adults). A tALP level > 120 U/L and/or PTH level > 6.8 nmol/L was taken as an indication of increased bone formation. Serum levels of 25-(OH)D were measured by radioimmunoassay (Immunodiagnostic Systems, Boldon, UK). This method measures 100% of 25-(OH)D_3, with 75% cross-reactivity with 25-(OH)D_2. Supplementation studies[10] and bone biopsy[11] suggest a level below 50 nmol/L is

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1 Maternal characteristics and sex of infant, according to attendance for postnatal follow-up (total *n* = 69)

	n	Attenders	Non-attenders	*P**
Mother's place of birth				0.008
Australia, New Zealand or Western Europe	23	10 (43%)	13 (57%)	
Africa (including one Afro-Caribbean)	30	24 (80%)	6 (20%)	
Other (Middle East or Indian subcontinent)	16	13 (81%)	3 (19%)	
Mother's first language				0.6
English	44	29 (66%)	15 (34%)	
Other language	25	18 (72%)	7 (28%)	
Mother's religion				0.4
Islam	62	41 (66%)	21 (34%)	
Other	7	6 (86%)	1 (14%)	
Mother's age				0.3
⩽ 29 years	37	23 (62%)	14 (38%)	
⩾ 30 years	32	24 (75%)	8 (25%)	
Sex of infant				0.001
Male	13	4 (31%)	9 (69%)	
Female	56	43 (77%)	13 (23%)	

* Based on χ^2 test.

		Attenders (*n* = 47)	Non-attenders (*n* = 22)	*P*†
Mother's vitamin D level in pregnancy (median [interquartile range], in nmol/L)	69	19.6 (16.7–22.9)	18.3 (13.1–23.5)	0.4

† Based on Mann–Whitney *U* test.

insufficient for bone health in adults and children. We defined 25-(OH)D sufficiency as levels ⩾ 50 nmol/L, insufficiency as levels 30–50 nmol/L, and deficiency as levels < 30 nmol/L.[12]

For children with a low vitamin D level and raised tALP and/or raised PTH level, an x-ray was offered.

Statistical analysis

As all laboratory measures and maternal age were not normally distributed, we present the results in the form of median and interquartile range (IQR), with intergroup comparisons by Kruskal–Wallis one-way ANOVA. Comparison of proportions was by a χ^2 test or Fisher's exact test.

RESULTS

Demographic data

Of 69 mother–infant pairs invited to participate in our postnatal study, 47 (68%) attended. The infants (gestation, 38–42 weeks) were seen at a median age of 7.7 months (range, 4.8–10 months). Maternal characteristics and sex of infant, for attenders versus non-attenders, are shown in Box 1. There was no association between maternal age, religion, first language or antenatal vitamin D level and attendance or month of testing.[12] Mothers were less likely to attend if they had a male infant or were of Australian or European background.

Among attenders, 19/47 (40%) were light-skinned; 37/41 Muslim women (90%) wore a hejab; and 22/47 women (47%) either did not have or did not use an outdoor family area. The median age of attenders was 30 years (IQR, 26–33).

Vitamin supplements

Although women with lower vitamin D levels in pregnancy were more likely to have been prescribed supplements, a quarter of the women attending postnatally were not prescribed supplements in pregnancy, and almost half did not take supplements as prescribed (Box 2). None continued supplements postnatally, although one woman had recently begun to take them again.

At the time of our study, two infants had recently been started on Penta-Vite (a multivitamin supplement that includes vitamin D_3).

Biochemical test results at postnatal follow-up

Mothers. Median levels (IQR) were: 25-(OH)D, 20.4 nmol/L (14.9–26.3 nmol/L) (unrelated to month of testing); tALP, 105 U/L (90–122 U/L); PTH, 5.3 nmol/L (4.1–9.7 nmol/L); calcium, 2.31 mmol/L (2.26–2.35 mmol/L); and phosphate, 1.16 mmol/L (1.09–1.34 mmol/L).

No woman had a 25-(OH)D level ⩾ 50 nmol/L, and 39/47 (83%) were vitamin D deficient (25-[OH]D < 30 nmol/L). Twenty-four of the 47 women (51%) had evidence of increased bone formation.

Infants. The first attempt at venepuncture was successful in 45 infants (no parents agreed to a second attempt). The median infant 25-(OH)D level was 63.5 nmol/L (IQR, 20.3–77.7). Of the 45 infants, 18 (40%) had levels < 50 nmol/L and 14 of these (31%) had levels < 30 nmol/L (1/4 aged 4–6 months, 7/20 aged 6–8 months and 6/21 aged 8–10 months). Evidence of increased bone formation was seen in 11/45 (24%) infants (1/4 aged 4–6 months, 6/20 aged 6–8 months and 5/21 aged 8–10 months).

Of 12 children invited for x-ray, 10 attended. One child had rickets. Another child with normal biochemical parameters, who was x-rayed because of flared wrists, a large fontanelle and a slight "rib rosary", had resolving rickets (the mother had been advised to give the child Penta-Vite, but had commenced it only a month before the clinic appointment). Incidentally, an older sibling of a normal infant had clinical features of rickets, which was confirmed biochemically and by x-ray.

Vitamin D deficiency and evidence of increased bone formation were more common in breastfed infants than those receiving formula milk (Box 3). All infants except one were having some solid foods.

DISCUSSION

Maternal vitamin D supplementation during pregnancy was erratic, and all 47 women attending for postnatal follow-up had vitamin D insufficiency. This was despite pro-

2 Prescription of vitamin D supplements during pregnancy, and compliance with taking supplements, among women who attended for postnatal follow-up (total *n* = 47)

Maternal vitamin D level in pregnancy (nmol/L)	Number of women (%) prescribed supplements	Number of women (%) prescribed supplements who took them as prescribed
< 16.2	16/16 (100%)	8/16 (50%)
16.2–21.0	14/16 (88%)	8/14 (57%)
21.1–29.9	5/15 (33%)	3/5 (60%)
	$P < 0.001$ (based on χ^2 test)	$P = 0.8$ (based on Fisher's exact test)

3 Vitamin D level and increased bone formation in infants, according to whether they were fed breastmilk or formula milk

	Age (median [IQR], in months)	Vitamin D level (median [IQR], in nmol/L)	Number (%) of infants with vitamin D deficiency*	Number (%) of infants with increased bone formation†
Fed formula milk only (*n* = 15)	7.7 (7.0–8.6)	78.2 (74.6–88.9)	0	0
Fed both breastmilk and formula milk (*n* = 14‡)	8.1 (7.2–8.8)	64.9 (50.6–74.8)	2/14 (14%)	3/14 (21%)
Fed breastmilk only (*n* = 16)	7.3 (7.3–8.6)	18.6 (14.7–30.7)	12/16 (75%)	8/16 (50%)
		$P < 0.001$§	$P < 0.001$¶	$P < 0.001$¶

IQR = interquartile range.

* Vitamin D deficiency was defined as serum levels < 30 nmol/L. † Serum levels of total alkaline phosphatase > 120 U/L and/or parathyroid hormone > 6.8 nmol/L were taken as markers of abnormal bone turnover. ‡ Two of 16 infants did not have a blood test. § Based on Kruskal–Wallis one-way ANOVA. ¶ Based on Fisher's exact test.

viding guidelines and making other efforts to educate hospital staff to screen and treat women at high risk and to encourage the women to continue vitamin D supplements postnatally. Ostelin 1000 (25-[OH]D_2), the only adult vitamin D supplement in Australia, was believed by some women to contain pork products. Now that its halal status has been approved (in May 2004), use of the supplement pre- and postnatally may increase.

Almost a third of the infants tested had vitamin D deficiency, a quarter had increased bone formation, and two had rickets. It is doubtful whether either case of rickets would have been diagnosed apart from our audit, raising the possibility that rickets is more prevalent in high-risk populations than is generally appreciated.

Breastmilk is a poor source of 25-(OH)D,[13] and breastfed infants are at higher risk of vitamin D deficiency than others.[14,15] Some national health authorities recommend universal supplementation of breastfed infants.[13] While we wholeheartedly endorse breastfeeding for all infants, this issue needs to be addressed in Australia. Penta-Vite is readily available for infant supplementation.

Our study has a number of weaknesses. The sample size was small, and children were seen at a variety of ages. A multilingual invitation letter may have encouraged more women to attend, although there was no evidence that the mother's first language influenced attendance. The test for vitamin D had only 75% cross-reactivity with 25-(OH)D_2, so 25-(OH)D levels may have been underestimated.

Nevertheless, there is a clear need for improved health education among populations at risk and their medical attendants. When a reliable body of data has been gathered on the vitamin D status of "low-risk" infants, we will need to reconsider recommendations for vitamin supplements for breastfed babies.

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COMPETING INTERESTS

None identified.

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