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Short Communication

Vitamin D status of pregnant and non-pregnant women of reproductive age living in Hanoi City and the Hai Duong province of Vietnam

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Abstract

Vitamin D insufficiency during pregnancy has been associated with a number of adverse outcomes for both mother and child. Vitamin D insufficiency has been well described in many populations of both pregnant and non-pregnant women of childbearing age, but there is a lack of data on women living in South-East Asia. We measured plasma 25-hydroxyvitamin D in a representative sample of pregnant ($n = 64$) and non-pregnant ($n = 477$) women (15–49 years) living in Hanoi City ($n = 270$) and rural Hai Duong Province ($n = 271$) in northern Vietnam. Mean 25-hydroxyvitamin D (95% confidence interval) concentration was 81 (79, 84) nmol L^{-1}. Mean 25-hydroxyvitamin D concentration differed between urban and rural (78 vs. 85 nmol L^{-1}; $P = 0.016$), farming and non-farming (89 vs. 77 nmol L^{-1}; $P < 0.001$) but not pregnant and non-pregnant or older vs. younger women. Only one woman had a 25-hydroxyvitamin D less than 25 nmol L^{-1}, a concentration indicative of vitamin D deficiency. Of the women, 7% and 48% of the women were vitamin D insufficient based on cut-offs for plasma 25-hydroxyvitamin D of 50 and 75 nmol L^{-1}, respectively. Mean plasma 25-hydroxyvitamin D concentrations of these Vietnamese women were much higher than those reported in other studies of pregnant and non-pregnant women in the region.

Keywords: vitamin D, 25-hydroxyvitamin D, women of childbearing age, pregnancy Vietnam.

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Introduction

Vitamin D insufficiency has been associated with a number of diseases including osteoporosis, cardiovascular disease as well as certain cancers and autoimmune conditions (Holick 2004; Garland *et al*. 2009). For women who become pregnant, vitamin D insufficiency has also been associated with a number of adverse outcomes for both mother and child. Pre-eclampsia, a leading cause of maternal morbidity, has been associated with low vitamin D status in a number of studies (Bodnar *et al*. 2007). Also, maternal vitamin D insufficiency increases the risk of rickets in her offspring and may increase the risk of type 1 diabetes (Hypponen *et al*. 2001), asthma (Erkkola *et al*. 2009) and osteoporosis (Javaid *et al*. 2006) later in life.

Vitamin D is obtained from skin synthesis through the action of ultraviolet (UV) light and from a few dietary sources. Not surprisingly, poor vitamin D status has been described in populations of pregnant (Judkins & Eagleton 2006; Newhook *et al*. 2009; Ginde *et al*. 2010) and non-pregnant women (Rushton *et al*. 2004; Rockell *et al*. 2006; Ginde *et al*. 2010) at

higher latitudes where there is little UV light in the winter months. However, there are increasing reports of vitamin D insufficiency in women at lower latitudes, particularly South Asia (Sachan *et al*. 2005; Islam *et al*. 2008) and the Middle East (Dawodu *et al*. 1998; Mishal 2001; Molla *et al*. 2005). There are relatively few reports on the vitamin D status of women of childbearing age living in South-East Asia. However, we reported that despite living very close to the equator – where UV exposure is highest worldwide – over 60% of women (18–40 years) surveyed in Jakarta, Indonesia (6°S) and Kuala Lumpur, Malaysia (2°N) were vitamin D insufficient based on plasma 25-hydroxyvitamin D (25OHD) concentrations less than 50 nmol L^{-1} (Green *et al*. 2007). Women in these convenience samples were urban, most were of high socio-economic status, and many had jobs that would have kept them indoors most of the day.

We recently conducted a nutrition survey of 555 pregnant and non-pregnant women (15–49 years) living in the urban city of Hanoi and the rural province of Hai Duong in northern Vietnam (21°N) (Vu *et al*. 2009). Given the mounting evidence of the importance of adequate vitamin D for women of reproductive age and the lack of population representative data on the vitamin D status of South-East Asian women, we measured 25OHD concentrations in this group of women.

Methods

The survey was conducted between October 2006 and January 2007. The Ethical Committee of Science of the National Institute of Nutrition of Vietnam approved the study, and all participants gave informed consent. Women (15–49 years) were recruited from Hai Duong Province and Hanoi City. In Hanoi City, a district (Hai Ba Trung) and then a ward (Quynh Mai) from within that district were randomly selected. We assigned family codes to all families in Quynh Mai ward that included women aged 15–49 years. From this list, the first family was selected by randomly choosing a family code. In the family selected, all non-pregnant women aged 15–49 years were invited to participate in the study. After selecting the first family, we used the 'random walking' method to approach other families, adding subjects to obtain 245 non-pregnant subjects stratified equally into seven age groups ($n = 35$ per group) as follows: 15–19, 20–24, 25–29, 30–34, 35–39, 40–44 and 45–49 years. In Hai Duong Province, Kim Thanh District was selected, and within this district, the Tuan Hung and Cong Hoa communes were randomly selected. Selection of women was as described for Hanoi City, while 154 ($n = 22$ per group) and 91 ($n = 13$ per group) participants were recruited in Tuan Hung and Cong Hoa communes, respectively. The primary aim of the original study was to determine folate status in non-pregnant women, and pregnant women were not included in the sampling design. However, when a pregnant woman was identified in a family and was approached, she was asked to participate in the study. Sixty-five pregnant women participated in this study.

Demographic details of the women were collected using questionnaires. Blood samples were taken by venepuncture into tubes containing EDTA following an overnight fast. Plasma 25OHD concentrations in blood were determined at the University of Otago, New Zealand, using radioimmunoassay kits

Key messages

- Vitamin D insufficiency during pregnancy may lead to adverse maternal and fetal outcomes.
- We have previously reported very high rates of vitamin D insufficiency in several countries in South-East Asia despite their proximity to the equator.
- We measured serum 25-hydroxyvitamin D (25OHD) concentrations in pregnant ($n = 65$) and non-pregnant ($n = 486$) women living in Hanoi City and rural Hai Duong Province.
- Mean 25OHD concentration was high at 90 nmol L^{-1} and was higher than that reported in other countries in the region.
- Nevertheless, many women were classified as vitamin D insufficient; 7 to 48% depending on cut-off.

(DiaSorin, Stillwater, MN, USA). Two levels of controls provided by the manufacturer were run in each assay. The inter-assay coefficient of variation based on repeated analysis of pooled controls for vitamin D was 9%.

Statistical analyses were performed using SPSS Statistics 18.0 for Macintosh (SPSS Inc., Chicago, IL, USA). Plasma 25OHD was log-transformed to normalize its distribution, and the estimates were back-transformed to geometric means with 95% confidence intervals (CIs). Univariate comparisons between participant characteristics and 25OHD concentration were made by analysis of variance and chi-squared test as appropriate. Multiple regression analysis was used to examine the independent relationship between participant characteristics and plasma 25OHD concentration. We used 25 nmol L^{-1} to define vitamin D deficiency (Mulligan *et al*. 2010) and two cut-offs to define vitamin D insufficiency, 50 and 75 nmol L^{-1} (Bischoff-Ferrari *et al*. 2006; Greer 2008; Food and Nutrition Board, Institute of Medicine 2010). Vitamin D deficiency is the concentration of 25OHD below, which the risk of osteomalacia increases markedly. Vitamin D insufficiency is a lesser form of inadequacy, generally not associated with osteomalacia, but may be associated with adverse health outcomes or suboptimal physiological responses. Multivariate logistic regression was used to determine the independent effects of participant characteristics and risk of insufficiency (<50 and <75 nmol L^{-1}).

Results

Five-hundred fifty-five women participated in the study, and the response rate was 100%. A 25OHD concentration was available for 541 women. Demographic characteristics of the participants are shown in Table 1. All but two women were ethnically Vietnamese (Kinh). Overall, about half of the women had completed high school with women from Hanoi being generally better educated than women from Hai Duong Province. Office clerk, worker, housewife and business owner were the most common occupations for Hanoi women, whereas the majority of women in Hai Duong Province reported their occupation as farmer. No woman reported using a vitamin D containing supplement.

Table 1. Participant characteristics ($n = 541$)

Descriptive	*n* (%)		
	All	Hanoi (urban)	Hai Duong (rural)
Number of participants	541 (100.0)	270 (50.1)	271 (49.9)
Age			
<30 years	241 (44.5)	120 (44.4)	121 (44.6)
≥30 years	300 (55.5)	150 (55.6)	150 (55.4)
Pregnant	64 (11.8)	33 (12.2)	31 (11.4)
Children	423 (78.2)	204 (75.6)	219 (80.8)
Occupation			
Office clerk	99 (18.2)	69 (25.6)	30 (11.1)
Worker	69 (12.8)	56 (20.7)	13 (4.8)
Housewife	65 (12.0)	59 (21.9)	6 (2.2)
Business owner	68 (12.6)	54 (20.0)	14 (5.2)
Farmer	186 (34.4)	0 (0.0)	186 (68.6)
Retired	11 (2.0)	10 (3.7)	1 (0.4)
Other	43 (8.0)	22 (8.1)	20 (7.4)
Highest education			
Less than grade 9	44 (8.2)	4 (1.5)	44 (16.2)
Completed grade 9	236 (43.6)	56 (20.7)	180 (66.4)
Completed grade 12	174 (32.2)	140 (51.9)	34 (12.5)
Completed university	87 (16.0)	70 (25.9)	16 (5.9)

The overall (geometric) mean 25OHD (95% CI) concentration was 81 (79, 84) nmol L^{-1}. The range was 20–280 nmol L^{-1}. There was no significant difference in mean 25OHD concentration between pregnant and non-pregnant or older vs. younger women. Mean 25OHD concentration was 7 nmol L^{-1} higher in rural vs. urban women ($P = 0.016$). Vitamin D status in farming women was 12 nmol L^{-1} higher compared with women who reported other occupations ($P < 0.001$). Multiple regression analysis in which other cofactors included in the univariate analysis were adjusted for did not alter the results with rural and farming women still having higher 25OHD concentrations than urban and non-farming women ($P < 0.001$), respectively.

Only one woman had a 25OHD less than 25 nmol L^{-1}, a concentration indicative of vitamin D deficiency. Of the women, 7% and 48% were vitamin D insufficient based on cut-offs for 25OHD of 50 and 75 nmol L^{-1}, respectively. Based on a cut-off of 50 nmol L^{-1}, urban, younger (less than 30 years), pregnant and non-farming women were more likely

Table 2. Plasma 25-hydroxyvitamin D concentration and prevalence insufficiency by selected characteristics

	n	Geometric mean (95% confidence interval)	*P*	Prevalence % vitamin D insufficiency			
				<50 nmol L^{-1}	*P*	<75 nmol L^{-1}	*P*
All	541	81 (79, 84)	–	7	–	48	–
Region							
Hanoi (urban)	270	78 (74, 82)	0.02	9	0.04	54	0.06
Hai Duong (rural)	271	85 (81, 89)		5		42	
Age (years)							
<30	241	78 (75, 83)	0.07	10	0.02	52	0.06
≥30	300	84 (80, 88)		5		45	
Pregnant							
Yes	64	75 (68, 83)	0.09	19	0.01	52	0.6
No	477	82 (79, 85)		6		48	
Occupation							
Farmer	186	89 (84, 95)	<0.001	2	0.001	35	<0.001
Other	355	77 (74, 81)		11		56	

to be vitamin D insufficient. Based on a cut-off of 75 nmol L^{-1}, urban and non-farming were more likely to be vitamin D insufficient compared with rural and farming women, respectively. Adjustment for other factors with logistic regression did not alter the results except that age ($P = 0.067$) was no longer a predictor of having a 25OHD less than 50 nmol L^{-1} (Table 2). Twenty-two women (4%) had a plasma 25OHD greater than 200 nmol L^{-1}. Eight of these women were farmers.

Discussion

To our knowledge, with over 500 participants, this is the largest population-based study of the vitamin D status of women of childbearing age living in South-East Asia. In contrast to other surveys of women of childbearing age in South-East Asia and elsewhere, the mean 25OHD concentration in our sample of Northern Vietnamese (21′N) women was high at over 81 nmol L^{-1}. In Hong Kong, which lies at a similar latitude (22′N), the mean 25OHD was only 34 nmol L^{-1} in a sample of 221 women (20–35 years) (Woo *et al*. 2007). Similarly, in urban equatorial women ($n = 504$; 18–40 years) living in Jakarta (6°S) and Kuala Lumpur (2°N), the mean 25OHD was only 48 nmol L^{-1}, around half that reported in the present study (Green *et al*. 2007). There are a number of possible explanations for these differences. The other studies recruited convenience samples of women who were likely of higher socio-economic status and may have had jobs and lifestyles that kept them inside a greater proportion of the time than the women in our study. Also, in contrast to Vietnam, Indonesian and Malaysian populations are predominately Muslim and these women may follow a dress custom that leaves little skin exposed. In Hong Kong, many women stay out of the sun to avoid tanning, a practice that may be less common in Vietnam (Kung & Lee 2006). Finally, vitamin D intake may be higher in Vietnam than the other countries. However, per capita consumption of fish in Vietnam, the chief source of dietary vitamin D, is similar to Indonesia and half that of Malaysia (Food and Agriculture Organization of the United Nations 2007).

Despite the generally high mean 25OHD, depending on the cut-off used, between 7% and 48% of women were vitamin D insufficient, potentially placing them at increased risk of adverse health outcomes. Although mean 25OHD did not differ between pregnant and non-pregnant women, the prevalence of vitamin D insufficiency (less than 50 nmol L^{-1}) was almost three times higher in pregnant women (19% vs. 6%; $P < 0.05$). Serum 25OHD concentrations in pregnancy are usually either similar to or lower than those in non-pregnant women (Salle *et al*. 2000). We acknowledge that there is a considerable debate about the most appropriate cut-off to

define vitamin D insufficiency and that the evidence base to support these cut-offs, particularly in pregnancy, is limited. Maternal 25OHD determines 25OHD concentration at birth. A cut-off of 50 nmol L^{-1} in pregnancy can be justified as infants and toddlers with 25OHD concentrations less than 50 nmol L^{-1} have shown evidence of bone demineralization (Gordon *et al*. 2008). The higher cut-off of 75 nmol L^{-1} is based largely on observational reports of associations between 25OHD and health outcomes in non-pregnant adults (Dawson-Hughes *et al*. 2005).

UV light exposure is the main determinant of 25OHD, and as expected, rural women would have higher plasma 25OHD concentrations, presumably, because they spend more time outdoors than urban women. Similarly, farming women had higher 25OHD concentrations than non-farming women. Further, rural and farming women were less likely to have a 25OHD less than 50 or 75 nmol L^{-1} suggesting that greater sunlight exposure may have protected against vitamin D insufficiency.

Strengths of our study include a representative sample and a 100% response rate. A limitation of our study is that we only sampled women in the late fall and early winter. Seasonal variation in vitamin D status is well described, but this is usually only pronounced at higher latitudes; nevertheless, it is possible that our results underestimate slightly the true vitamin D status of women in this survey. The UV index in Hanoi (21°N) ranges from six (high) in January to 12 (extreme) in July, indicating that seasonal differences in UV do exist. We did not assess dietary intake of vitamin D and thus, are unable to quantify the effect of dietary intake on vitamin D status. Nevertheless, fish consumption in Vietnam appears to be low, and there are few other dietary sources of vitamin D. Finally, although our sample is a representative of Hanoi and Ha Duong Province, we can not extrapolate our findings to the rest of Vietnam. Vietnam is a country that is geographically and climatically diverse, and it is possible that vitamin D status is different in other parts of the country. Indeed, in a study that included 432 non-pregnant women (18–87 years) in Ho Chi Minh City in Southern Vietnam, mean 25OHD was 75 nmol L^{-1}, somewhat lower than in our study (Ho-Pham *et al*. 2011). However, the prevalence of insufficiency (<75 nmol L^{-1}) was similar to our study at 46%.

In conclusion, the mean serum 25OHD concentrations of northern Vietnamese women were much higher than those reported in other studies of pregnant and non-pregnant women in the region. The obvious explanation for this is that Vietnamese women obtain more UV light exposure than their counterparts in neighbouring countries in the region. It would be interesting to determine the lifestyle behaviours that are leading to a better vitamin D status in Vietnam. Despite having better vitamin D status than women in nearby countries, nearly 50% were vitamin D insufficient based on a 25OHD of less than 75 nmol L^{-1}. Strategies may be needed to improve the vitamin D status of this population.

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Conflicts of interest

JMT works for and TJG has consulted for Fonterra Brands Limited, Auckland New Zealand. There were no other conflicts of interest.

Contributions

TG, VTTH, NTL and CMS were responsible for the study design and implementation and secured the funding for the work. VTTH and NTL supervised the fieldwork including blood collection and processing. TG and CMS supervised the vitamin D analysis. TG, JT and JM interpreted the data and wrote the first draft. All authors had input into the final version of the paper.

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