

# Maternal and neonatal vitamin D status at birth in black South Africans

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**Background.** Vitamin D deficiency (VDD) in pregnant women has been associated with adverse pregnancy and neonatal outcomes. 25-hydroxyvitamin D (25(OH)D) levels are affected by numerous factors, including vitamin D intake, skin pigmentation, latitude and season of the year; they therefore vary by race and country. Vitamin D status in pregnant women and their offspring in South Africa (SA) is not well established.

**Objectives.** To assess vitamin D status by measuring serum 25(OH)D in pregnant black SA women and their offspring in Johannesburg (latitude 26°S) and to assess whether vitamin D status is affected by maternal HIV infection.

**Methods.** We prospectively enrolled pregnant women and their healthy neonates, and measured 25(OH)D in maternal and cord blood at delivery. Pregnant women were stratified by their HIV status. Predictors of maternal and neonatal VDD (levels <30 nmol/L) were assessed using multiple logistic regression analysis.

**Results.** A total of 291 pregnant women and their healthy neonates were enrolled over a 21-month period. Mean (standard deviation) maternal and cord blood 25(OH)D levels were 57.0 (29.7) and 41.9 (21.0) nmol/L and the prevalence of VDD was 15.9% and 32.8%, respectively. On average, concentrations of 25(OH)D in cord blood were ~80% of those in the mother. There was no association between cord 25(OH)D and gestational age, but levels were associated with birth weight ( $p < 0.001$ ). There were no differences in maternal or cord blood 25(OH)D levels between those HIV-infected or uninfected. The predictor of VDD in mothers was giving birth in winter (odds ratio (OR) 2.87, 95% confidence interval (CI) 1.47 - 5.61), and in neonates the predictors were maternal age (OR 16.5, 95% CI 1.82 - 149), being born in winter (OR 3.68, 95% CI 2.05 - 6.61), being born by caesarean section (OR 4.92, 95% CI 1.56 - 15.57) and being of low birth weight (OR 1.99, 95% CI 1.13 - 3.50).

**Conclusions.** Among black SA women delivering in Johannesburg, about one in six mothers and one in three neonates have 25(OH)D levels indicative of VDD. Maternal HIV status appears not to affect levels of 25(OH)D in either the mother or her neonate. Research on the effects of VDD on the outcomes of pregnancy and the best methods to combat the high prevalence of VDD in women of childbearing age in the SA context is required.

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Globally, women generally have poor vitamin D status during pregnancy.<sup>[1,2]</sup> Maternal vitamin D deficiency (VDD) has been associated with an increased risk of adverse maternal and neonatal outcomes.<sup>[3]</sup> The fetus is entirely dependent on transplacental acquisition of maternal 25-hydroxyvitamin D (25(OH)D) to maintain its vitamin D status, so neonatal vitamin D status at birth is directly related to maternal status. Vitamin D is a prohormone that is either ingested or produced in the skin from 7-dehydrocholesterol through the influence of ultraviolet B (UVB) radiation. Cholecalciferol (vitamin D<sub>3</sub>) and dietary vitamin D are transported to the liver, where they are metabolised to form 25(OH)D, which is the major circulating vitamin D metabolite. 25(OH)D is converted in the kidney to 1,25-dihydroxyvitamin D (1,25(OH)<sub>2</sub>D), the active form of vitamin D. 1,25(OH)<sub>2</sub>D binds to a single nuclear type 2 (vitamin D) receptor to facilitate the activation or suppression of target genes.<sup>[4]</sup>

Serum 25(OH)D levels provide an excellent measure of overall vitamin D status. They reflect both intake from the diet and the

amount contributed by skin synthesis. The levels are strongly associated with the degree of skin pigmentation and exposure to UVB radiation, which is influenced by skin coverage, latitude and season of the year.<sup>[5-7]</sup> Rich sources of dietary vitamin D such as fortified foods, fish oil and organ meats are often not affordable to women from poor communities. In the absence of these dietary sources of vitamin D, sunlight therefore becomes the major source of vitamin D. In blacks, skin melanin decreases the penetration of UVB through the skin, limiting the production of vitamin D. The high melanin content of the skin and an inadequate intake of dietary vitamin D could therefore put black women at risk of developing VDD. Other strong determinants of serum 25(OH)D levels are latitude and the season of the year. Serum 25(OH)D levels are higher during summer than winter months and in populations closer to the equator. However, these responses are also influenced by genetic factors, duration and dose of UVB exposure, and baseline serum 25(OH)D levels.<sup>[8,9]</sup> It is therefore important to report levels of 25(OH)D for different communities based on skin pigmentation, latitude and seasons of the year.

## Objectives

Levels of 25(OH)D in pregnant mothers and their offspring have not been well studied in sub-Saharan Africa, especially in settings where the majority of pregnant women are black and women frequently have HIV infection. HIV infection could potentially affect the transfer of 25(OH)D through altering maternal-fetal exchange.<sup>[10]</sup> It is therefore important to determine the prevalence of VDD in neonates, not only in segments of the population in which VDD is likely to be high, but also in settings where the prevalence of HIV is high. The objectives of this study were to determine the 25(OH)D levels of pregnant women and their infants at birth and to assess whether levels are affected by maternal HIV status.

## Methods

### Study design and setting

We undertook a prospective cohort study at Chris Hani Baragwanath Academic Hospital (CHBAH) in Soweto, Johannesburg, South Africa (SA), between March 2013 and November 2014. Soweto has a latitude of 26°S, an average elevation of 1 600 m and a temperate climate. The average daily sunshine hours vary between 7 hours 30 minutes and 9 hours 45 minutes over the year. All pregnant women attending antenatal care at CHBAH are counselled and offered HIV testing as part of standard care. The HIV prevalence has been ~29% since 2006.<sup>[11]</sup>

### Study population and procedures

All mothers and their neonates who were delivered at CHBAH during weekdays between 08h00 and 14h00 were eligible for the study. Neonates who had major congenital abnormalities, were assessed to have clinical signs of infection or had been prescribed antibiotics by the attending doctor were excluded. Only those whose mothers had consented were enrolled. Selection of patients was based on a convenience sample; the first two consenting mothers screened between 08h00 and 14h00 on weekdays who delivered neonates meeting the inclusion criteria were enrolled. Following informed consent from mothers, blood was collected from the mother and the umbilical cord of her neonate. Blood samples were centrifuged at 2 000 g for 5 minutes and separated serum was refrigerated at -70°C until the assays were performed at the end of enrolment. 25(OH)D levels were measured in both maternal and cord blood samples.

### Data collection

The maternal data collected included race, age, gravidity, HIV status, and mode and month of delivery, and the neonatal data included birth weight, gestational age, Apgar score and health status. 25(OH)D levels were measured using the Liaison chemiluminescent immunoassay (DiaSorin, Italy). The inter-assay coefficient of variation (CV) for lower and higher controls was 10% and 9%, respectively, and the intra-assay CV was 8% and 6%, respectively. VDD was defined as a 25(OH)D concentration of <30 nmol/L.<sup>[12]</sup> To assess seasonal variation in 25(OH)D concentrations, the seasons were divided as follows: summer (December through February), autumn (March through May), winter (June through August) and spring (September through November).

### Sample size estimation

As a prospective survey to assess vitamin D status, we estimated that we needed to enrol a cohort of 320 pregnant women. This was based on a prevalence of VDD (25(OH)D <30 nmol/L) of 3.4% reported in an abstract from a pilot study conducted in pregnant women delivering at CHBAH,<sup>[13]</sup> and having 2% confidence limits and a 95% confidence level.

## Data analysis

In order to assess the relationship between 25(OH)D levels and HIV status, mothers were stratified into HIV-negative and HIV-positive, and infants into HIV-unexposed and HIV-exposed (but not necessarily infected). Infants were grouped according to gestational age (<30, 30 - 34, 35 - 37 and >37 weeks) and weight (<1 500, 1 500 - 1 999, 2 000 - 2 499 and ≥2 500 g) categories. Correlations between cord blood and maternal 25(OH)D concentrations were assessed using the Pearson test. Multivariate logistic regression analyses were performed to determine factors associated with VDD.

## Ethical considerations

Ethics approval to conduct the study was obtained from the University of the Witwatersrand Human Research Ethics Committee (ref. no. M120651), and the management of the hospital gave its approval. Written informed consent for study inclusion was obtained from the mothers for themselves and their newborns.

## Results

### Study population

Out of a total of 6 179 deliveries conducted between 08h00 and 14h00 on weekdays over a 21-month period, a total of 696 pregnant women were approached for informed consent, with 75 (10.8%) refusing consent. Neonates of 276 mothers were assessed to be sick by the attending doctor and were therefore excluded. A total of 345 mothers with 360 well neonates were enrolled, and 291 mothers and neonates were included in the final analysis (Fig. 1). Neonates who were enrolled on the same day after the first two neonates had been enrolled were excluded ( $n=69$ ). There were more women enrolled during the autumn and winter months than other months, as the enrolment period was 21 months which included two autumn, winter and spring seasons, and there was slow enrolment towards the end of the study because we lost the services of our research assistant.

### Maternal characteristics

Maternal HIV status was known for all but one mother, and 138 (47%) were HIV-positive. The majority of the neonates (98%) were

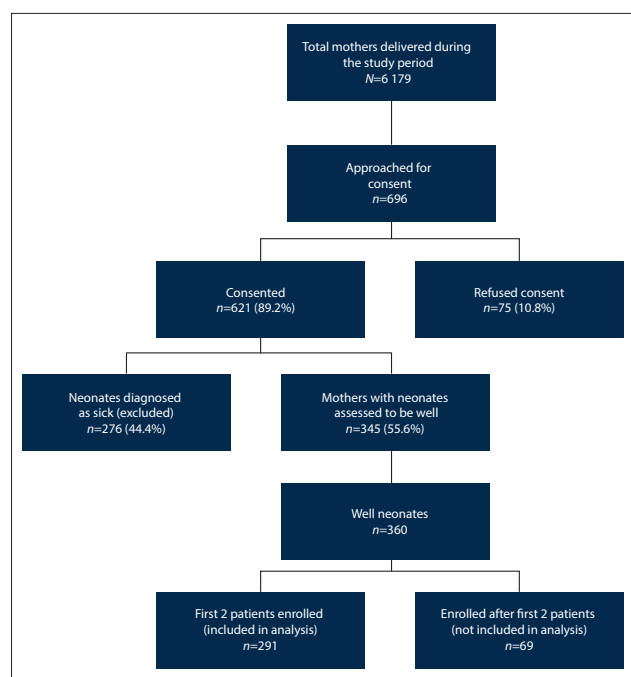


Fig. 1. Mothers and neonates enrolled in the study.

born to black African women, with a mean (standard deviation (SD)) age of 28 (6) years; 70% were multiparous and 94% delivered vaginally (Table 1). There was no association between demographic variables and HIV status except for maternal age, which on average was 4 years younger in HIV-negative mothers than in HIV-positive mothers.

**25(OH)D levels in pregnant women**

The mean (SD) 25(OH)D concentration in pregnant women was 57.0 (29.7) nmol/L. There were no statistical significant differences in 25(OH)D levels between HIV-positive and negative mothers (58.8 (31.2) v. 55.5 (28.3) nmol/L, respectively;  $p>0.05$ ) (Table 2). Maternal levels of 25 (OH)D did not differ by duration of gestation or neonatal birth weight. Maternal levels were also not associated with HIV status even after adjusting for gestational age ( $p=0.410$ ). VDD (serum 25(OH)D <30 nmol/L) was present in 16% of mothers.

**25(OH)D levels in cord blood**

The mean cord blood 25(OH)D level (SD) was 41.9 (21.0) nmol/L, and there was no statistically significant difference between HIV-exposed and unexposed neonates (40.7 (21.2) v. 42.8 (20.9) nmol/L;  $p=0.172$ ) (Table 2). VDD was noted in 33% of neonates overall. There was no statistically significant difference in the prevalence

of neonates with 25(OH)D deficiency among the HIV-exposed and unexposed mothers (36.2% v. 29.8%;  $p=0.129$ ), even after stratifying them into preterm ( $\leq 37$  weeks) and term ( $>37$  weeks), or into low birth weight ( $<2\ 500$  g) and normal birth weight ( $\geq 2\ 500$  g).

**Transplacental transfer of 25(OH)D**

On average, concentrations of 25(OH)D in cord blood were ~80% (mean (SD) cord-to-maternal 25(OH)D ratio 0.79 (0.45)) of those in the mothers (Table 3). There was no association between the fraction of 25(OH)D transferred and gestational age or maternal HIV status. However, the fraction increased significantly as birth weight increased ( $p<0.001$ ). On average, the ratio increased by 30% for every 1 000 g increase in birth weight. There was a significant correlation between maternal and cord serum 25(OH)D levels with  $r=0.53$  (Fig. 2), and there was a strong association between VDD in mother and infant ( $p<0.001$ ).

**25(OH)D levels in relation to the season of the year**

Mean 25(OH)D levels were highest in summer and lowest in winter for both mothers and their infants (Fig. 3). The proportion of mothers with VDD increased from 7% in summer to 27% in winter, while the prevalence of VDD in cord blood increased from 22% in summer to 60% in winter. Pregnant women were three times more

**Table 1. Characteristics of enrolled mothers and their healthy neonates**

	Overall (N=291*)	HIV-positive (N=138)	HIV-negative (N=152)	p-value
<b>Maternal characteristics</b>				
Black African, n (%)	286 (98.3)	137 (99.3)	149 (97.4)	0.427
Maternal age (years), mean (SD)	28 (6)	30 (6)	26 (6)	<0.001
Gravidity, n (%)				0.127
1	86 (29.6)	33 (23.9)	52 (34.2)	
2 - 4	188 (64.6)	95 (68.8)	93 (61.2)	
>4	17 (5.8)	10 (7.2)	7 (4.6)	
Mode of delivery, n (%)				0.314
Vaginal	273 (93.8)	132 (95.7)	140 (92.1)	
Caesarean section	18 (6.2)	6 (4.3)	12 (7.9)	
Season of the year at birth, n (%)				0.267
Autumn	113 (38.8)	47 (34.1)	66 (43.4)	
Winter	73 (25.1)	36 (26.1)	37 (24.3)	
Spring	57 (19.6)	27 (19.6)	29 (19.1)	
Summer	48 (16.5)	28 (20.3)	20 (13.2)	
<b>Infant characteristics</b>				
Birth weight (g), mean (SD)	2 819 (544)	2 815 (527)	2 824 (562)	0.88
Birth weight categories (g), n (%)				0.795
<1 500	0	0	0	
1 500 - 1 999	15 (5.2)	6 (4.3)	9 (5.9)	
2 000 - 2 499	84 (28.9)	41 (29.7)	42 (27.6)	
≥2 500	192 (66)	91 (65.9)	101 (66.4)	
Gestational age (weeks), mean (SD)	37 (2)	37 (2)	37 (2)	0.731
Gestational age categories (weeks), n (%)				0.99
<30	2 (0.7)	1 (0.7)	1 (0.7)	
30 - 34	40 (13.7)	19 (13.8)	20 (13.2)	
35 - 37	101 (34.7)	49 (35.5)	52 (34.2)	
>37	148 (50.9)	69 (50.0)	79 (52.0)	
Apgar score, median (IQR)				
1 minute	9 (9 - 9)	9 (9 - 9)	9 (9 - 9)	0.912
5 minutes	10 (10 - 10)	10 (10 - 10)	10 (10 - 10)	0.965

SD = standard deviation; IQR = interquartile range.  
\*HIV result unknown for 1 mother.

**Table 2. Levels of 25(OH)D in maternal and cord blood**

	Serum 25(OH)D concentrations (nmol/L), mean (SD)			Proportion with VDD, n/N (%)		
	HIV-infected (N=138)	HIV-uninfected (N=152)	All (N=291*)	HIV-infected (N=138)	HIV-uninfected (N=152)	All (N=291*)
<b>Maternal</b>						
All	58.8 (31.2)	55.5 (28.3)	57.0 (29.7)	23/137 (16.8)	23/152 (15.1)	46/290 (15.9)
Gestational age (weeks)						
<30	31.8 (n/a)	71.5 (n/a)	51.6 (28.1)	0/1 (0)	0/1 (0)	0/2 (0)
30 - 34	54.3 (32.8)	46.2 (21.8)	49.9 (27.1)	3/18 (16.7)	4/20 (20.0)	7/39 (17.9)
35 - 37	57.1 (34.2)	52.2 (26.7)	54.6 (30.5)	9/49 (18.4)	11/52 (21.2)	20/101 (19.8)
>37	61.5 (28.8)	59.9 (30.3)	60.7 (29.5)	11/69 (15.9)	8/79 (10.1)	19/148 (12.8)
Season						
Autumn	59.3 (26.1)	55.4 (23.5)	57.0 (24.5)	9/46 (19.6)	5/66 (7.6)	14/112 (12.5)
Winter	41.2 (20.1)	43.5 (17.6)	42.4 (18.8)	12/36 (33.3)	8/37 (21.6)	20/73 (27.4)
Spring	59.9 (33.9)	55.2 (34.4)	57.3 (33.7)	0/27 (0)	9/29 (31)	9/57 (15.8)
Summer	79.2 (35.8)	78.6 (36.4)	79.0 (35.7)	2/28 (7.1)	1/20 (5)	3/48 (6.2)
<b>Cord blood</b>						
All	40.7 (21.2)	42.8 (20.9)	41.9 (21.0)	50/138 (36.2)	45/151 (29.8)	95/290 (32.8)
Gestational age (weeks)						
<30	13.8 (n/a)	27.8 (n/a)	20.8 (9.8)	1/1 (100)	1/1 (100)	2/2 (100)
30 - 34	47.2 (29.6)	34.0 (17.2)	41.1 (24.8)	7/19 (36.8)	9/20 (45.0)	16/40 (40.0)
35 - 37	36.7 (18.3)	42.5 (22.7)	39.7 (20.8)	19/49 (38.8)	19/52 (36.5)	38/101 (37.6)
>37	42.2 (20.0)	45.3 (20.2)	43.9 (20.1)	23/69 (33.3)	16/78 (20.5)	39/147 (26.5)
Birth weight categories (g)						
<1 500	-	-	-	-	-	-
1 500 - 1 999	38.8 (25.5)	30.7 (17.3)	34.0 (20.5)	3/6 (50.0)	6/9 (66.7)	9/15 (60.0)
2 000 - 2 499	39.4 (24.6)	37.8 (22.8)	38.9 (23.7)	17/41 (41.5)	19/41 (46.3)	36/83 (43.4)
≥2 500	41.4 (19.4)	45.8 (19.7)	43.8 (19.7)	30/91 (33.0)	20/101 (19.8)	50/192 (26.0)
Season						
Autumn	45.6 (18.5)	49.8 (20.2)	48.1 (19.5)	9/47 (19.1)	10/66 (15.2)	19/113 (16.8)
Winter	30.1 (19.2)	34.3 (16.0)	32.2 (17.6)	22/36 (61.1)	18/37 (48.6)	40/73 (54.8)
Spring	39.0 (19.6)	33.3 (18.7)	36.7 (19.5)	12/27 (44.4)	13/28 (46.4)	25/56 (44.6)
Summer	47.8 (24.6)	48.3 (24.4)	48.0 (24.2)	7/28 (25.0)	4/20 (20.0)	11/48 (22.9)

25(OH)D = 25-hydroxyvitamin D; SD = standard deviation; VDD = vitamin D deficiency; n/a = not applicable.  
\*HIV result unknown for 1 mother.

**Table 3. Serum 25(OH)D cord-to-mother ratio**

	HIV-infected (N=138), mean (SD)	HIV-uninfected (N=152), mean (SD)	Overall (N=291*), mean (SD)
All	0.77 (0.42)	0.85 (0.42)	0.82 (0.42)
Gestational age categories (weeks)			
<30	0.44 (n/a)	0.39 (n/a)	0.41 (0.03)
30 - 34	0.92 (0.62)	0.78 (0.33)	0.86 (0.49)
35 - 37	0.75 (0.40)	0.86 (0.33)	0.81 (0.37)
>37	0.75 (0.36)	0.87 (0.49)	0.82 (0.44)
Birth weight categories (g)			
<1 500	-	-	-
1 500 - 1 999	0.60 (0.24)	0.65 (0.20)	0.63 (0.21)
2 000 - 2 499	0.77 (0.48)	0.75 (0.39)	0.77 (0.44)
≥2 500	0.78 (0.40)	0.91 (0.44)	0.85 (0.42)

25(OH)D = 25-hydroxyvitamin D; SD = standard deviation; n/a = not applicable.  
\*HIV result unknown for 1 mother.

likely to be vitamin D deficient if delivered in winter compared with the other seasons.

**Factors associated with VDD in cord blood**

On multiple regression analysis, the predictor of VDD in pregnant women at the time of delivery was giving birth during winter (odds

ratio (OR) OR 2.87, 95% confidence interval (CI) CI 1.47 - 5.61 (Table 4). The predictors of VDD in cord blood were maternal age >20 years (OR 16.5, 95% CI 1.82 - 149.0; *p*=0.013), delivery in winter (OR 3.68, 95% CI 2.05 - 6.61; *p*<0.001), low birth weight (OR 1.99, 95% CI 1.13 - 3.50; *p*=0.017) and being born by caesarean section (OR 4.92, 95% CI 1.56 - 5.57; *p*=0.003) (Table 5).

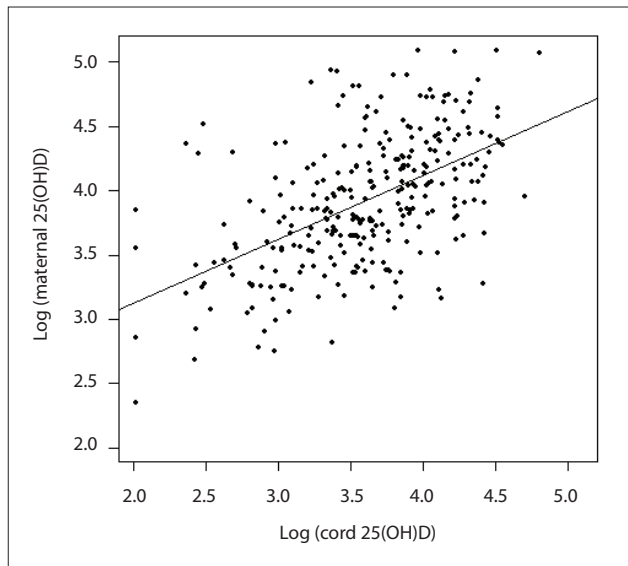


Fig. 2. Correlation between maternal and cord blood 25(OH)D concentrations ( $r=0.53$ ,  $p<0.001$ ). (25(OH)D = 25-hydroxyvitamin D.)

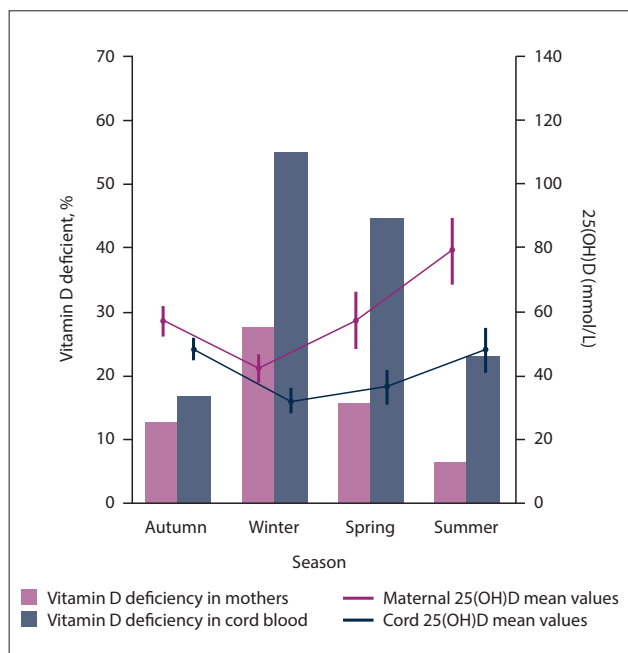


Fig. 3. Maternal and cord blood 25(OH)D levels according to different seasons of the year. (25(OH)D = 25-hydroxyvitamin D.)

## Discussion

The increasing number of reports of VDD being associated with adverse obstetric and neonatal outcomes suggests that the extent of this problem should be assessed for each community or population in which VDD may be prevalent. Serum 25(OH)D reflects the adequacy of vitamin D intake and cutaneous production and is therefore used for assessment of vitamin D status. In this study, we assessed serum 25(OH)D in women and their offspring at delivery in Johannesburg, SA (latitude 26°S), throughout the year in order to assess the prevalence of VDD and the factors associated with this deficiency.

In a cohort of 291 pregnant women, we found that the mean (SD) 25(OH)D level was 57.0 (29.7) nmol/L, and that about one in six pregnant women (16%) were vitamin D deficient at

delivery. The maternal serum 25(OH)D levels in this study were similar to those reported in non-pregnant adult black African women in Johannesburg, in whom the mean 25(OH)D level was 58.3 nmol/L,<sup>[14]</sup> and to levels reported in African Americans in the USA,<sup>[15-17]</sup> but higher than those reported from Asian countries, where the mean is <40 nmol/L.<sup>[18]</sup> Compared with studies in other parts of sub-Saharan Africa, the mean value in the present study was lower.<sup>[19-22]</sup> In Nigeria, the mean 25(OH)D level was reported to be 90 nmol/L in pregnant women not practising purdah (use of veils by women).<sup>[19]</sup> In East Africa, mean serum 25(OH)D levels in pregnant women ranged from 91.9 nmol/L in rural western Kenya<sup>[22]</sup> to 141.9 nmol/L and 147.7 nmol/L in the Sengerema and Maasai ethnic groups, respectively.<sup>[20]</sup> Likely reasons for these geographical differences are related to differences in sun exposure and its zenith angle, but they could also be due to the different methodologies used to determine 25(OH)D.

In the present study, it was also noted that levels of 25(OH)D varied by season, with levels during summer being almost double those in winter (82.9 v. 41.8 nmol/L). Not surprisingly, the prevalence of VDD among mothers also varied seasonally, with VDD being four times more common in winter than in summer (27% v. 7%). Numerous other studies have reported similar seasonal variations.<sup>[23-26]</sup> The present study and these other studies confirm that sun exposure is a major determinant of vitamin D status in humans. The proportion of women with deficiency in this study was much higher than that reported in a pilot study from the same institution (Ranchod *et al.*<sup>[13]</sup>), where deficiency was noted in only 3.4% of women. The reasons for this difference are unclear, but it may be due to fewer women being studied, and the data only being collected in autumn, despite this being one of the seasons when 25(OH)D levels are expected to be high.

The mean 25(OH)D concentration in cord blood was 41.9 nmol/L, and it correlated with maternal serum 25(OH)D concentrations ( $r=0.53$ ). This finding is similar to other studies that have consistently reported a correlation between cord blood 25(OH)D and maternal concentrations.<sup>[15,17,23,27-29]</sup> Although the correlation of  $r=0.53$  is similar to that reported by Yu *et al.*<sup>[30]</sup> in the UK ( $r=0.45$ ) and higher than that reported by Thomas *et al.*<sup>[27]</sup> from New Zealand ( $r=0.30$ ), it is lower than those in many other studies, which reported correlations ranging from 0.63 to 0.89.<sup>[15,17,23,29]</sup> The main factors influencing cord blood concentrations of 25(OH)D in the present study were maternal serum 25(OH)D, season of the year, low birth weight and caesarean section.

Overall, the prevalence of VDD in neonates was ~33%. This prevalence is lower than that reported in African-American neonates, which varied from 46% to 65%.<sup>[15,31-33]</sup> The prevalence in white neonates has been reported to be much lower at 4 - 11%.<sup>[15,31,34,35]</sup> These variations between racial groups reflect differences in 25(OH)D levels between black and white mothers. In our study, the ratio of cord to maternal 25(OH)D improved with increasing birth weight, suggesting a role for placental function maturity in the transfer of 25(OH)D, levels of fetal vitamin D-binding protein or changes in fetal rates of hydroxylation or catabolism. Higher maternal 25(OH)D levels have previously been shown to be significantly associated with higher placental volume,<sup>[36]</sup> and vitamin D insufficiency has been associated with low birth weight.<sup>[37,38]</sup> It is unclear why neonates born by caesarean section were more likely to have VDD, despite adjustment for seasons. Possible reasons could be related to the indication for caesarean section. In our study setting, one of the common indications for caesarean section is pre-eclampsia, the prevalence of which has been associated with VDD.<sup>[39-41]</sup> The low

**Table 4. Univariate and multivariate analysis for factors associated with vitamin D deficiency in mothers**

Variable	n (%)	Univariate <i>p</i> -value	OR (95% CI)	Multivariate <i>p</i> -value
Maternal age (years)				
<20	23 (7.9)	Ref	-	-
20 - 35	228 (78.4)	0.684	-	-
>35	40 (13.7)	0.862	-	-
Mother black African	286 (98.3)	0.989	-	-
Mother primigravida	86 (29.6)	0.375	-	-
Mother HIV-infected	138 (47.6)	0.701	-	-
Delivered in winter months	73 (25.1)	0.002	2.87 (1.47 - 5.61)	0.002
Preterm (<37 weeks)	104 (35.7)	0.91	0.54 (0.24 - 1.26)	0.156
Low birth weight (<2 500 g)	99 (34.0)	0.148	2.18 (0.97 - 4.9)	0.058
Caesarean section	18 (6.2)	0.923	-	-

OR = odds ratio; CI = confidence interval.

**Table 5. Univariate and multivariate analysis for factors associated with vitamin D deficiency in cord blood**

Variable	Univariate <i>p</i> -value	OR (95% CI)	Multivariate <i>p</i> -value
Maternal age (years)			
<20		Ref	Ref
20 - 35	0.012	16.48 (1.82 - 148.97)	0.013
>35	0.089	9.13 (0.9 - 92.93)	0.062
Mother black African	0.729	-	-
Mother primigravida	0.748	-	-
Mother HIV-infected	0.246	-	-
Delivered in winter months	<0.001	3.68 (2.05 - 6.61)	<0.001
Preterm (<37 weeks)	0.123	-	-
Low birth weight (<2 500 g)	0.001	1.99 (1.13 - 3.5)	0.017
Caesarean section	0.003	4.92 (1.56 - 15.57)	0.007

OR = odds ratio; CI = confidence interval.

rate of caesarean section in this cohort is probably due to the cases of caesarean section being selected out because of the enrolment process, as enrolment took place soon after delivery, when neonates delivered by caesarean section were likely to be receiving specialised care and attention in resuscitation areas.

The higher than expected proportion of HIV-infected women in the cohort (41% v. 29% among all women delivering at the hospital) is the most likely reason for the higher proportion of low-birth-weight infants in the study than in the overall hospital delivery population. HIV infection in pregnancy is associated with an increased prevalence of low-birth-weight infants.<sup>[42]</sup> HIV infection has been associated with VDD in a number of studies.<sup>[43-47]</sup> This association has been explained by possibly reduced maternal sunlight exposure owing to severity of the infection, or increased susceptibility of HIV infection due to VDD-associated immunosuppression. Treatment with antiretrovirals has been reported to improve 25(OH)D levels.<sup>[48,49]</sup> In the present study, we did not find any association between HIV infection and VDD, possibly because most HIV-infected mothers were on antiretroviral therapy and well.

### Study strengths and limitations

The strengths of this study include the large number of patients enrolled and the fact that the study was conducted across the four seasons of the year. Further, the laboratory that measured the 25(OH)D levels has participated for many years in an external quality assurance programme (DEQAS) that monitors the accuracy

of the assay used. A limitation of this study is that environmental and nutritional factors such as the use of vitamin D supplements, sunscreens and sunlight exposure, which could influence vitamin D status, were not assessed.

### Conclusions

The present study has highlighted the generally poor vitamin D status of black women and their neonates delivering at CHBAH, with one in six women and one in three neonates being VDD. A marked seasonal variation in 25(OH)D levels in both the mothers and their neonates was noted, indicating the importance of the contribution of sunlight exposure and epidermal synthesis of vitamin D in the mother in maintaining vitamin D status. These data raise concerns about the lack of a policy in SA recommending routine vitamin D supplementation of black mothers during pregnancy, as has been proposed in an international consensus statement and by the Institute of Medicine.<sup>[12,50]</sup> Although no data are available on the consequences of VDD during pregnancy and lactation on mothers and their infants in SA, there is a growing body of international literature to suggest that low vitamin D status may have effects on pregnancy-induced hypertension, preterm deliveries, fetal growth and birth weight, neonatal bone mass, risk of asthma, neonatal hypocalcaemia and epigenetics.<sup>[51]</sup> Future studies should investigate the factors influencing vitamin D status in mothers and their offspring, the maternal and fetal/neonatal outcomes associated with poor vitamin D status, and the most efficacious way of correcting maternal VDD through supplementation during pregnancy.

**Declaration.** This study was part of the work towards SCV's PhD degree.

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**Author contributions.** SCV: study conceptualisation, study design, collection of data, data analysis and interpretation, drafted and revised manuscript, approved submission of manuscript. AI: statistical data analysis and interpretation, revised and reviewed manuscript, approved submission of manuscript. SAM: study design, data interpretation, revised and reviewed manuscript, approved submission of manuscript. JMP: study conceptualisation, study design, data interpretation, revised and reviewed manuscript, approved submission of manuscript.

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