Prevalence of vitamin D deficiency in older South Africans with and without hip fractures and the effects of age, body weight, ethnicity and functional status

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Background: Vitamin D plays an important role in many physiological and pathological processes, including bone metabolism. Vitamin D deficiency is common worldwide, but there are few data in older South Africans.
Objectives: This study aimed to determine vitamin D status in older adults with and without hip fractures and the effect of demography, body mass index (BMI) and functional status on vitamin D levels.
Methodology: In a secondary analysis, the association between 25(OH) vitamin D levels, obtained from 327 subjects (151 with fractures and 176 controls), and age, gender, ethnicity, BMI and functional status, was explored using Student's *t*-test, a chi-square test, regression analysis and ANOVA.
Results: In the total cohort, vitamin D deficiency and insufficiency was present in 27% and 38%, respectively. While vitamin D levels decreased with age, this was not significant ($p = 0.082$). There was a significant association between vitamin D and BMI ($p = 0.023$), the physical maintenance scale ($p = 0.002$) and independent activities of daily living ($p = 0.001$). Mean vitamin D levels in fracture subjects was significantly lower than controls (39.4 ± 23.1 nmol/l vs. 50.1 ± 23.3 nmol/l, $p = 0.00$) and vitamin D deficiency and/or insufficiency was significantly more common in the fracture group compared with controls (75.5% vs. 56.8%, $p = 0.00$). There was no association with gender or ethnicity.
Conclusions: Vitamin D deficiency is common in this population, especially in those with hip fractures. Contrary to other studies, increasing BMI was associated with higher vitamin D levels. This suggests that poor health status as indicated by a low BMI and poorer functional status is associated with lower vitamin D levels. The high prevalence of vitamin D deficiency and/or insufficiency in the cohort strongly argues for universal vitamin D supplementation in older adults, especially those at risk for osteoporotic fractures.

Keywords: Vitamin D, older adults, South Africa, hip fracture

Introduction

Vitamin D, a steroid pre-hormone, is thought to play an important role in many physiological and pathological processes.[1] Its role in bone health is best established with deficiency being associated with osteoporosis and osteomalacia as well as decreased neuromuscular and psychomotor function.[2–6] In older adults, calcium and vitamin D co-supplementation decreases fracture and fall risk.[7] The Institutes of Medicine (IOM) Committee recommends that a serum concentration of 25-hydroxyvitamin D (25(OH)D) of 50 nmol/l is sufficient for bone and overall health in healthy individuals.[8]

Several studies have looked at the prevalence of vitamin D deficiency, but the global prevalence is unknown, as data from many geographical regions, including Africa, are limited.[9,10] Additionally, there is poor consensus regarding the serum levels defining vitamin D adequacy, and differing laboratory assay methods make standardisation and comparison between studies difficult.[11,12]

In a systematic review comprising 168 000 subjects from more than 195 countries, 37.3% of the studies reported mean 25(OH)D values below 50 nmol/l, with the highest values observed in North America.[9] Age-related differences were observed in the Asia/Pacific and Middle East/Africa regions, but gender showed no influence worldwide.

Risk factors for low 25(OH)D levels include limited sunshine exposure, poor diet and physiological and pathological problems with 25(OH)D metabolism. Lips compared 25(OH)D levels across Europe, the Middle East and Asia and identified low sunshine exposure, darker skin pigmentation, and high latitude as well as obesity, malabsorption and advanced age as risk factors for vitamin D deficiency.[13] Immigrant populations from the Middle East and Asia living in Europe emerged as high-risk groups. Within Europe, serum 25(OH)D levels were higher in northern countries compared with the sunny south, postulated to be due to a higher intake of vitamin D in the form of fatty fish, fortified foods and supplements.[13] Similarly, Rizzoli *et al.* in a large study of post-menopausal women with osteoporosis from the same geographical areas including Latin America and the Pacific Rim found similar associations with vitamin D deficiency, namely, non-Caucasian ethnicity, obesity, higher latitude, minimal sunshine exposure and poor general health as well as a low level of education.[14] There was no seasonal variation in 25(OH)D levels but clothing and cultural habits, similar to findings by Mithal *et al.*,[15] were identified as strong influencers of 25(OH)D concentration. Mithal also described low socioeconomic status, urban living, advancing age and female gender as consistent risk factors.[15]

There are limited data on vitamin D status in older South Africans. Interest in vitamin D, however, dates back to 1978 when Pettifor reported that the seasonal variation in 25(OH)D levels, in elderly subjects with neck of femur fractures in Johannesburg, was more likely due to a change in clothing habits in the winter months than overall sunlight exposure.[16] Almost two decades later, the seasonal variation was reported to be more marked in Cape Town compared with Johannesburg.[17] In Cape Town in the same year, Charlton *et al.* reported vitamin D deficiency

(defined as 25(OH)D < 25 nmol/l) and severe deficiency (< 20 nmol/l) in 17% and 7.5% respectively, in Coloured subjects older than 65 years.[18] More recently, George *et al.* found a prevalence of vitamin deficiency (defined as 25(OH)D ≤ 30 nmol/l) in 3% and 15% of African and Asian Indian adults respectively, in Johannesburg.[19]

There have been no previous studies on vitamin D status in the eThekwini region. While eThekwini and Johannesburg both have a subtropical climate, eThekwini experiences milder winters and is at sea level. This study was undertaken to determine the vitamin D status and the effects of ethnicity, age, gender, body mass index (BMI) and functional status on 25(OH)D levels in older adults in eThekwini.

Methods
Ethical approval for the study was granted by the University of KwaZulu-Natal's Biomedical Research Ethics Committee (BREC number BE 362/16).

This study is a secondary analysis of data collected in a prospective, descriptive study of osteoporotic hip fractures, in five public sector hospitals in the eThekwini region of KwaZulu-Natal, which provide orthopaedic services, namely King Edward VIII, Addington, RK Khan, Mahatma Gandhi Memorial and Prince Mshiyeni Memorial Hospitals. Between August 2011 and July 2013, consecutive subjects with a new minimal trauma hip fracture who were able to give informed consent were enrolled from these hospitals. Exclusion criteria included fractures distal to the lesser trochanter, pathological and high-impact fractures, and the refusal or inability to give informed consent. Age, ethnicity and gender-matched controls were recruited from volunteers with no prior history of osteoporosis or hip fracture.

Of the 200 hip fracture subjects and matched controls, 25(OH)D levels were available in 327 subjects (151 subjects with hip fractures and 176 controls). Demographic data, a fall history (subjects were asked whether they had had a fall in the preceding year), body mass index (BMI), functional assessment and biochemical results were recorded using a standardised, structured questionnaire.

When possible, weight was measured on a balance-beam scale and height using a stadiometer. The standard formula (BMI = weight (kg) / height (m^2)) was used to calculate BMI, which was then categorised according to the World Health Organization (WHO) categories for adults aged 25 years and older as: underweight ≤ 18.9 kg/m^2, ideal 19–24.9 kg/m^2, overweight 25–29.9 kg/m^2 and obese ≥ 30 kg/m^2.[20]

Lawton's Physical Self-Maintenance Scale (PSMS) and the Instrumental Activities of Daily Living (IADL) scale were used to assess functional status. The PSMS assesses the subject's competence in toileting, feeding, dressing, grooming, locomotion and bathing. The minimum score is 0 (unable to do any of these basic activities) and the maximum achievable score is 24 (independent for all activities).[21] The IADL assesses the individual's ability to live independently. The score for IADL ranges from 10 to 30.[21]

The high-performance chromatography (HBLC) based Chromasystems diagnostic kit (ThermoFisher Scientific, Waltham, MA, USA) was used to measure 25(OH)D at the Central National Health Service laboratory in Johannesburg, and levels were

Table 1: IOM classification of vitamin D status in relation to 25(OH)D levels

25(OH)D levels (min–max range) nmol/l**	Category ng/ml*	
< 30	< 12	Deficient
30 to < 50	12 to < 20	Insufficient
≥ 50	≥ 20	Sufficient

25(OH)D: 25 hydroxyvitamin D; IOM: Institutes of Medicine.

classified as sufficient, insufficient and deficient according to the IOM categories (Table 1).[8]

Statistical analysis
The data were analysed using IBM® SPSS® 21 (IBM Corp, Armonk, NY, USA) and Microsoft Excel 2016 (Microsoft Corp, Redmond, WA, USA). The significance for all tests was set at $p < 0.05$. For descriptive data, means and standard deviations were used. Demographic characteristics were expressed as frequencies and percentages. To compare variables inferential statistics were applied including Student's t-test for numerical variables, a chi-square test for categorical variables, Fisher's exact test where frequencies were small and regression analysis and ANOVA.

Results

Demographic and biochemical characteristics
Demographic data of the 327 subjects, 151 (46.2%) with hip fractures and 176 (53.8%) ethnicity- and gender-matched controls, are given in Table 2. There was no statistically significant difference in age, gender and ethnicity between the two groups. BMI was available in 285 of these subjects (109 fracture subjects and 176 controls). Significantly more than expected of the fracture group were underweight or had an ideal weight, while significantly more than expected of the control group were overweight or obese ($p < 0.0005$).

Table 2: Characteristics of fracture and control subjects

Item	Fracture subjects n (%)	Controls n (%)	Total n (%)	*p*-value
Number	151 (46.2)	176 (53.8)	327 (100)	0.237*
Age (years)	73.7 ± 8.6	72.6 ± 7.9	73.1 ± 8.2	
Gender:				
Male	48 (14.7)	54 (16.5)	102 (31.2)	0.830**
Female	103 (31.5)	122 (37.3)	225 (68.8)	
Ethnicity:				
African	56 (17.1)	66 (20.2)	122 (37.3)	0.939**
Indian	95 (29.1)	110 (33.6)	205 (62.7)	
BMI (kg/m^2):				
≤ 19	22 (7.7)	3 (1.1)	25 (8.8)	< 0.0005**
19.1–24.9	60 (21.1)	44 (15.4)	104 (36.5)	
25–29.9	18 (6.3)	57 (20)	75 (26.3)	
≥ 30	9 (3.2)	72 (25.3)	81 (28.4)	
PSMS (Mean ± SD)	13.2 ± 2.1	13.8 ± 1.0	13.5 ± 1.60	0.001*
IADL	22.0 ± 4.9	25.4 ± 3.50	23.7 ± 4.5	< 0.0005*
Positive fall history	106 (70)	101 (57)	207 (63.3)	0.685**

Data shown as number (%) or mean ± SD. BMI: body mass index; IADL: instrumental activities of daily living; PSMS: physical self-maintenance scale. Tests used for *p*-values: independent samples t-test* and chi-square**.

The mean score for the pre-morbid physical self-maintenance assessment was significantly lower in fracture subjects (13.18 ± 2.08) compared with controls (13.82 ± 1.02, $p = 0.001$. Similarly, fracture subjects had a significantly lower mean IADL score (21.96 ± 4.89) compared with controls (25.35 ± 3.50), $p < 0.0005$. There was no significant difference in the previous fall history between both groups.

Relationship between vitamin D levels and demographic variables in the total cohort

In regression analysis, 25(OH)D, as a continuous variable, decreased with age, but this did not reach statistical significance ($p = 0.082$), nor was there any difference with ethnicity and gender. However, BMI was a significant predictor of 25(OH)D status ($\beta = 0.481$, $p = 0.023$) (Figure 1) as was functional status. The PSMS had a significant effect on 25(OH)D levels (B = 2.572, 95% confidence = (0.955–4.099), $p = 0.002$), namely a decreasing physical maintenance score was associated with decreasing 25(OH)D levels. Similarly, IADL was also a significant predictor of 25(OH)D levels (B = 0.961, $p = 0.001$).

Relationship between mean vitamin D levels and age, gender, ethnicity and BMI in fracture and control subjects

The mean 25(OH)D level for the total group at 45.2 ± 23.8 nmol/l was in the insufficient range. Hip fracture subjects had significantly lower mean 25(OH)D levels (39.4 ± 23.1 nmol/l) than did controls (50.1 ± 23.3 nmol/l), $p < 0.0005$ (Table 3).

Mean 25(OH)D levels were significantly lower in the fracture groups for each category of age, gender and ethnicity. For BMI, the only significant difference in 25(OH)D levels between fracture and control groups was in the ideal BMI category where levels were lower in the fracture groups (38.5 ± 18.9 nmol/l) than controls (49.1 ± 25.4 nmol/l), $p = 0.016$ (Table 3).

Relationship between vitamin D categories and age, gender, ethnicity and BMI in the total cohort, fracture and control groups

When testing for relationships between the categorised measure for 25(OH)D and the demographic variables age, gender and ethnicity, no significant relationships were found either across the full cohort (Table 4) or for each group (fracture and control) separately (Table 5).
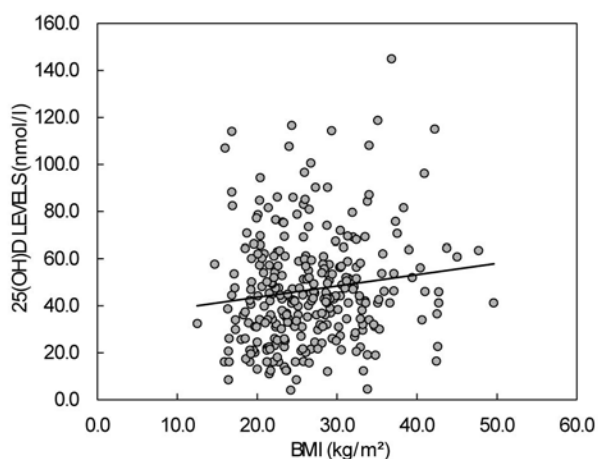

Figure 1: Scatter diagram showing relationship between 25hydroxyvitamin D (25(OH)D) levels and body mass index (BMI) in total cohort (superimposed regression line).

Table 3: Comparison of mean vitamin D levels according to age, gender, ethnicity and body mass index in fracture and control subjects.

Item	Mean 25(OH)D ± SD		*p*-value
	Fractures	Controls	
	39.4 ± 23.1	50.1 ± 23.3	< 0.0005
Age (years):			
60–69	43.0 ± 26.9	52.7 ± 26.0	0.049
70–79	38.5 ± 21.6	48.9 ± 21.5	0.005
> 80	36.5 ± 20.1	47.2 ± 20.9	0.031
Gender:			
Male	34.7 ± 21.3	51.1 ± 21.7	0.000
Female	41.6 ± 23.6	49.7 ± 24.0	0.012
Ethnicity:			
African	38.9 ± 24.0	51.7 ± 22.7	0.003
Indian	39.7 ± 22.6	49.2 ± 22.7	0.004
BMI (kg/m^2):			
< 19	43.8 ± 29.2	54.7 ± 24.9	0.546
19–24.9	38.5 ± 18.9	49.1 ± 25.4	0.016
25–29.9	42.5 ± 19.7	50.2 ± 21.5	0.180
> 30	53.8 ± 31.4	50.5 ± 23.7	0.706

Data shown as mean ± SD. BMI: body mass index. Independent samples t-test used for *p*-values.

Relationship between vitamin D categories and falls

Of the total cohort of 327 subjects, 164 (50.2%) had had at least one previous fall. There was no statistically significant relationship between 25(OH)D status and a history of previous falls ($p = 0.685$) (Table 6).

Discussion

In this, the first study to compare 25(OH)D levels in older persons with and without fragility fractures in South Africa, vitamin D deficiency and insufficiency is reported in 27% and 38%, respectively. This is substantially higher than that found in previous South African studies. In 1996 Charlton et al. reported lower frequencies of vitamin D deficiency and moderately severe deficiency at 17% and 7.5%, respectively, in older subjects of mixed ancestry.[18] However, this may have been an underreporting as their cut-off value of < 25 nmol/l was lower than that currently recommended by the IOM (i.e. < 30 nmol/l). Despite using the IOM recommendations, George et al. also found a much lower prevalence of 3.0% in African and 15.0% in Asian Indian sub-groups. Of note is that their study participants were healthy and younger (mean age 41.6 years in Africans and 43.5 years in Indians) and probably more physically active than in the current study.[22]

The higher prevalence of vitamin D deficiency in this study is therefore likely to be due to the older age of the participants and the inclusion of fracture subjects. Several studies have reported the association of 25(OH)D deficiency with age,[2,23,24] due to physiological and pathological mechanisms including medications such as anticonvulsants and glucocorticoids.[25,26] In a systematic review of worldwide vitamin D status, age-related differences in 25(OH)D levels were observed in the Asia/Pacific and Middle East/Africa but not in other geographical areas.[9] The cause for this was unclear but may have been due to lower vitamin D consumption or cultural practices determining sun exposure in these areas. In the present study, although 25(OH)D levels decreased with age in the total cohort, this did not reach statistical significance. Possible reasons for this include the fact that all subjects were over the age of 60 years,

Table 4: Comparison of vitamin D status across age, gender, ethnicity and BMI groups for the total cohort.

Item	*n*	Deficient *n* (%)	Insufficient *n* (%)	Sufficient *n* (%)	*p*-value
			25(OH)D status		
Total cohort	327	89 (27)	125(38)	113 (35)	
Age groups:					
60–69	120	29 (24.2)	44 (36.7)	47 (39.2)	0.437
70–79	136	40 (29.4)	49 (36)	47 (34.6)	
≥ 80	71	20 (28.2)	32 (45.1)	19 (26.8)	
Gender:					
Male	102	29 (28.4)	42 (41.2)	31 (30.4)	0.559
Female	225	60 (26.7)	83 (36.9)	82 (36.4)	
Ethnicity:					
African	122	35 (28.7)	44 (36.1)	43 (35.2)	0.811
Indian	205	54 (26.3)	81 (39.5)	70 (34.1)	
BMI (kg/m^2):					
< 19	25	9 (36)	8 (32)	8 (32)	0.211
19–24.9	104	29 (27.9)	42 (40.4)	33 (31.7)	
25–29.9	75	14 (18.7)	31 (41.3)	30 (40)	
> 30	81	13 (16)	31 (38.3)	37 (45.7)	

Data given as number and (%). 25(OH)D: 25 hydroxyvitamin D; BMI: body mass index.
Institutes of Medicine classification used for vitamin D categories. Statistical analysis using chi-square.

Table 5: Comparison of vitamin D status, across age, gender, ethnicity and BMI categories, in fracture and control subjects

	Fractures				**Controls**			
	25(OH)D status				**25(OH)D status**			
Item	Deficient *n* (%)	Insufficient *n* (%)	Sufficient *n* (%)	*p*-value	Deficient *n* (%)	Insufficient *n* (%)	Sufficient *n* (%)	*p*-value
Total group	63 (41)	51 (33.8)	37 (24.5)		26 (14.8)	74 (42)	76 (43.2)	
Age groups:								
60–69	20 (40.8)	13 (26.5)	16 (32.7)	0.467	9 (12.7)	31 (43.7)	31 (43.7)	0.725
70–79	27 (42.9)	22 (34.9)	14 (22.2)		13 (17.8)	27 (37)	33 (45.2)	
≥ 80	16 (41)	16 (41)	7 (17.9)		4 (12.5)	16 (50)	12 (37.5)	
Gender:								
Male	22 (45.8)	19 (39.6)	7 (14.6)	0.149	7 (13)	23 (42.6)	24 (44.4)	0.902
Female	41 (39.8)	32 (31.1)	30 (29.1)		19 (15.6)	51 (41.8)	52 (42.6)	
Ethnicity:								
African	26 (46.4)	17 (30.4)	13 (23.2)	0.657	9 (13.6)	27 (40.9)	30 (45.5)	0.882
Indian	37 (38.9)	34 (35.8)	24 (25.3)		17 (15.5)	47 (42.7)	46 (41.8)	
BMI (kg/m^2):								
< 19	9 (39.1)	6 (26.1)	8 (34.8)	0.699	0 (0)	2 (66.7)	1 (33.3)	0.949
19–24.9	21 (35)	25(41.7)	14 (23.3)		8 (18.2)	18 (40.9)	18 (40.9)	
25–29.9	6 (35.3)	5 (29.4)	6 (35.3)		8 (14)	25 (43.9)	(42.1)	
> 30	3 (33.3)	2 (22.2)	4 (44.4)		10 (13.9)	29 (40.3)	33 (45.8)	

Data given as number and (%). 25(OH)D: 25 hydroxyvitamin D; BMI: body mass index. Vitamin D status categorised according to the Institutes of Medicine classification. Chi-square tests used to compare groups.

Table 6: Relationship between 25(OH)D levels and fall history in the total cohort

25(OH)D status	Yes *n* (%)	No *n* (%)	Total *n* (%)	*p*-value
	History of falls			
Deficient	48 (29.3)	41 (25.1)	89 (27.2)	0.685
Insufficient	60 (36.6)	65 (39.9)	125 (38.2)	
Sufficient	56 (34.1)	57 (35)	113 (34.6)	
Total	164	163	327	

Data shown as number and (%). 25(OH)D: 25 hydroxyvitamin D. Statistical analysis using chi-square.

thus not allowing for comparison with younger persons and the relatively small number of subjects in the higher age groups, especially in the over 80 years group.

In addition, this study included fracture subjects and the relationship between vitamin D deficiency and diminished skeletal health has been widely reported.[27–29] In this study, mean 25(OH)D levels were significantly lower in fracture subjects compared with controls across all age groups, gender and ethnicity. Nevertheless, a significant proportion of both groups, albeit higher in the fracture group (74.8%) compared with the controls (56.8%), were either 25(OH)D deficient or insufficient.

Ethnicity has been found to influence 25(OH)D levels in studies conducted in and outside South Africa;[16,30–32] however, this was not the case in the present study. Ethnic differences have been explained by polymorphisms in the 25(OH)D receptor as well as its interaction with genetics, epigenetics and environmental factors.[1] Socioeconomic factors such as less access to vitamin D-rich foods and supplements may explain the lack of ethnic differences in the present study as well as the exclusion of White and Coloured subjects from the analysis.

Although more severe deficiency has previously been reported in women,[14,33,34] there was no gender difference in 25(OH)D levels in this study. However, like the findings of Steele et al.,[35] men with fractures had the lowest mean 25(OH)D levels, suggesting that 25(OH)D deficiency in men may play a more important role in skeletal health. The decreased 25(OH)D levels due to decreased testosterone in healthy men is thought to be due to ageing and changes in visceral adiposity.[36]

The relationship between 25(OH)D levels and body composition is less clear. Obesity has been reported as a risk factor for vitamin D deficiency in several studies and a meta-analysis of 34 studies demonstrated a significant, albeit weak, inverse correlation between serum 25(OH)D levels and BMI in adults.[37–40] On the other hand, Sulistyoningrum et al. showed a negative association between visceral fat and 25(OH)D concentrations in South Asian women compared with Europeans.[41] However, George et al. found that total body fat and visceral and subcutaneous fat were not predictors for 25(OH)D concentrations in South Africans of African and Indian descent, who were largely overweight.[22] By contrast, in this study, BMI was a significant predictor of 25(OH)D status in the total cohort, i.e. 25(OH)D levels increased with increasing BMI. Of note is that significantly more than expected of the fracture group were underweight or had an ideal weight than controls, and that 25(OH)D levels were significantly lower in fracture subjects in the ideal BMI group. This finding suggests that a lower BMI, as an indicator of overall poor health or chronic illnesses and organ dysfunction, may be associated with decreased 25(OH)D concentrations.

Further support for the relationship between vitamin D deficiency and poor overall health is the reported association between vitamin 25(OH)D deficiency and decreased handgrip strength, body sway and trunk stability as well as increased fall risk.[5,6,34] Similarly, in this study 25(OH)D levels decreased with decreasing physical performance, with both basic activities and instrumental activities of daily living. However, no relationship between 25(OH)D status and falls was observed.

Conclusion
In this cross-sectional study in the eThekwini region of South Africa, a high prevalence of vitamin D deficiency and insufficiency is reported in older adults with and without hip fractures. Vitamin D deficiency in this population is associated with lower body mass index, advancing age and a decreased functional status. With almost two-thirds of this cohort being either vitamin D deficient or insufficient, a strong case for universal vitamin D supplementation, at least in the older population, can be argued.

Limitations
This study enrolled Indian and African subjects who accessed public health services only and may reflect participants from lower socioeconomic status and thus overestimate the prevalence of vitamin D deficiency and insufficiency. The inclusion of White and Coloured subjects and those from the private healthcare sector would have made these findings more generalisable to the local eThekwini population.

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