VITAMIN D LEVELS OF ANESTHETISTS FROM 'SUNNY' SOUTH AFRICA: AN OCCUPATIONAL EXPOSURE STUDY

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Abstract

Background: Vitamin D influences a number of physiological processes. There is a resurgence of interest in vitamin D and its' far-reaching clinical effects. Anesthetists work indoors for most of their work hours and thus are at risk for vitamin D deficiency.

This study aimed to investigate the influence that these long indoor working hours have on anesthetists' vitamin D levels by describing serum 25-hydroxy vitamin D levels of trainee anesthetists in an academic anesthesiology department in South Africa, and to compare the factors influencing these vitamin D levels.

Methods: We conducted a single centre occupational observational study to describe the serum 25-hydroxy vitamin D (25(OH)D) levels of anesthesiology trainees working in a university training centre in South Africa. Data were collected over a period of one month during winter in 2013. Each participant completed a questionnaire and provided a blood sample for analysis of 25-hydroxyvitamin D levels.

Results: Of the 92 anesthetists that were tested, three were excluded due to laboratory error resulting in a total sample of 89. The median (IQR) 25-hydroxy vitamin D was 43.8 nmol/l (26 - 76), with 51 of 89 (57.30%) anesthetists meeting the criteria for being vitamin D insufficient. Factors that had a statistically significant influence on the vitamin D level were ethnicity ($p<0.001$) and use of multivitamins ($p=0.01$).

Conclusion: The insufficient vitamin D levels of anesthetists in this study puts them at risk for pathology far beyond bone health. Inadequate vitamin D levels are a problem, even in "sunny" African climates.

Keywords: Anesthetists, South Africa, Vitamin D.

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Introduction

Vitamin D has a profound impact on physiological processes in the body. Not only does vitamin D deficiency interfere with the attainment of peak bone mass but it has a number of previously unrecognised effects which include immune modulation,[1] increased risk of certain cancers, autoimmune conditions, cardiovascular disease and mental illness.[1,2] Recent meta-analyses[3,4] and a placebo controlled trial,[5] have however brought the validity of these effects into question.

Anesthetists work indoors for most of their working hours. Despite South Africa commonly being regarded as a land of sunshine,[6] South African anesthetists have long working hours and are often not exposed to this sunshine. This places them at risk for vitamin D deficiency. Vitamin D deficiency is a global problem[1,7,8] that has been studied extensively in colder climates[9-11] and is also shown to be prevalent in warmer climates.[12-14] There is no research in this field for medical personnel in Africa.

A prospective single centre occupational observational study was conducted to describe the serum 25-hydroxy vitamin D (25(OH)D) levels of trainee anesthetists (referred to as anesthetists in this study) working at a South African university medical training centre, and to compare the factors influencing these levels.

Methods

This was a single centre occupational observational study. Approval to conduct the study was granted by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand (M130305, 03/05/2013). The study was conducted in adherence to the principles of the Declaration of Helsinki[15] and the South African Good Clinical Practice Guidelines and Good Laboratory Practice Guideline.[16] Written informed consent was obtained from all participants.

Selection and Description of Participants

Patients and the general public were not involved in this study. The study population was anesthetists working in an academic Anesthesiology training centre in South Africa. A convenience sampling method was used. To be included in the study anesthetists had to have been working in the department for at least one month. Pregnant anesthetists, those who had travelled to sun-rich destinations in the month prior to the study, as well as those taking medication or having diseases interfering with vitamin D metabolism were excluded.

Exposure assessment

Data were collected over a period of one winter month (mid-July to mid-August 2013). The participants completed a novel questionnaire which was developed by the authors and underwent face and content validation. The questionnaire included the following information: participant characteristics, dietary intake and supplementation with vitamin D and quantification of sun exposure (area of skin exposed and duration over the last month). Quantification of sun exposure was based on the participants answering of the questionnaire which collated area of skin exposure and duration. This was then compared to the unit of comparison of UV radiation- a “Minimal Erythemal Dose”. Cultural attire like “veiling” was not specifically recorded in the questionnaire, but was incorporated into the aforementioned quantification of sun exposure.

Technical Information

Each participant had five millilitres of blood collected in a standardised manner into an ethylenediaminetetraacetic acid blood specimen tube. The specimens were refrigerated in a portable cooler between 2 and 8 °C and were delivered to an accredited chemical pathology laboratory within four hours of collection. The samples were then frozen and processed in batches. The laboratory used nmol/l, which is the S.I unit, as the unit of measurement to report results. The unit of measurement used by the IOM is ng/ml. The conversion factor for ng/ml to nmol/l is 2.5 (2.496).

High Performance Liquid Chromatography (HPLC) was performed on the blood samples to determine 25(OH)D levels using a Shimadzu®

Nexera X2 Ultra performance liquid chromatography system with a photodiode array detector (Shimadzu®, Japan). The samples were extracted and analysed as per the "25 OH Vitamin D Recipe® kit" (Recipe® Munich, Germany) method where the vitamin D_2 and D_3 fractions of 25(OH)D are separated and then combined to give total 25(OH)D. Fifty micromillitres (µl) of the extracted sample was injected onto the chromatographic system where the vitamin D fractions were detected at 264nm. A three-point calibration curve was run with every sample and two controls (one low level and one high level) were performed on every tenth sample.

The system was validated prior to running the sample with correlation coefficients r2=92% for linearity. The limit of detection was 1.2 nmol/l for $25(OH)D_3$ and 1.8 nmol/l for $25(OH)D_2$. The limit of quantitation was 7 nmol/l for $25(OH)D_3$ and 9 nmol/l for $25(OH)D_2$. Intraday and interday precisions were reported as 7% and 9% for $25(OH)D_3$ and 6.5% and 8% for $25(OH)D_2$.

The Institute of Medicine (IOM)[17] classification of vitamin D status in free living healthy adults, with regard to bone health was used in this study:

vitamin D deficiency: 25(OH)D < 30 nmol/l (<12 ng/ml)

vitamin D inadequacy: 25(OH)D of 30 to 50 nmol/l (12 to 20 ng/ml)

vitamin D sufficiency: 25(OH)D > 50 nmol/l (>20 ng/ml)

Statistical analysis

Using available literature[9,10,18] on vitamin D insufficiency in medical personnel, in consultation with a biostatistician, a minimum sample size of 81 participants was calculated to estimate the expected proportion of insufficiency of 30% to an accuracy of within 10%.

Data were captured on Microsoft Office Excel 2010® spread sheets and analysed in consultation with a biostatistician using using Statistica® Version 12.5. Frequencies, percentages, means, standard deviations, median and interquartile range were used. Chi-squared tests were used to compare factors influencing vitamin D levels. A p-value of <0.05 was regarded as statistically significant. Following initial data analysis, the "others" ethnic group was excluded from the statistical analysis as this group had only eight participants and was too small for statistical calculation.

Results

During the data collection period, 92 blood samples were collected and tested by HPLC to determine 25(OH)D levels. Three samples were excluded due to laboratory error resulting in a total sample of 89.

The mean (SD) age of the study population was 31.33 (± 4.32) years. Further demographic characteristics are shown in Table 1.

Table 1
Demographic characteristics of participants

			Frequency	(%)
Sex	Female		45	50.56
	Male		44	49.44
Ethnic Group	Black		20	22.47
	Indian		26	29.21
	Causcasian		35	39.33
	Arabic	"Others"	4	4.49
	Asian	"Others"	3	3.37
	Coloured	"Others"	1	1.12
BMI (kg/m2)	<25		55	61.80
	≥25		34	38.20

Anesthetists' median (IQR) 25(OH)D levels were 43.8 nmol/l (26-76). Vitamin D status of the study population is shown in Table 2, and demonstrates that there were 28 (31.46%) anesthetists that could be categorised as being vitamin D deficient. A further 23 (25.84%) were in the inadequate category. The combination of the deficient and inadequate categories into an insufficient category, as is common in the literature, reveals that 51 (57.30%) anesthetists were vitamin D insufficient.

Table 2: Vitamin D status of anesthetists

Vitamin D status	Frequency	(%)	
Deficient	28	31.46	**Insufficient**
Inadequate	23	25.84	
Sufficient	38	42.70	

The factors influencing anesthetists' vitamin D levels are listed and compared in Table 3.

Discussion

The integral role that vitamin D plays in homeostasis spreads far beyond calcium and bone health.[1,2] In apparently "sunny"' climates the impact of inadequate sun exposure is often overlooked or under investigated. Anesthetists work long hours and exclusively indoors, and therefore are at risk for having decrease sun exposure even in "sunny" climates. Our study found the anesthetists' median 25(OH)D levels to be 43.8 nmol/l, with 57.30% of participants found to be vitamin D insufficient. Among the factors influencing anesthetists' vitamin D levels, a statistically significant association between ethnicity and vitamin D status was found.

Working indoors is known to be a risk factor for vitamin D insufficiency.[7] Doctors also have an increased risk of deficiency due to their long working hours. Sowah and colleagues[19] reviewed vitamin D levels of different occupations and found that residents and medical students have the lowest levels of vitamin D among healthcare professionals. These authors also reported that shift working was an additional risk factor.[19] Other studies among doctors found 25%,[9] 30%[18] and 47%[10] to be insufficient. In a 2014 study in anaesthesia personnel in Iceland and Wisconsin, United States of America (USA), the authors reported 34.9% and 25%, respectively, of their subjects to be insufficient.[20] In Turkey, only 4.8% of anaesthesia personnel studied were found to be vitamin D sufficient. All of these studies were performed at northern latitudes during or at the end of winter.

The vitamin D levels of anesthetists in our southern hemisphere study were not normally distributed with a median (IQR) 25(OH)D of 43.8 nmol/l (26-76). The prevalence of vitamin D insufficiency in our study was found to be 57.30%, despite South Africa having a "sunny" climate with a UV index of 5 during winter.[21] Similarly, Mendoza and colleagues[13] found 75% of the doctors in their study during the Mexican summer to be insufficient, despite the fact that Mexico City had the highest UV index figures in studies among doctors.

Growdon and colleagues[9] concluded from their

Table 3
Comparison of factors influencing anesthetists' vitamin D status

Factor		**Insufficient** Frequency (%)	**Sufficient** Frequency (%)	**P value**
Ethnicity	Black	14 (70)	6 (30)	
	Indian	21 (80.77)	5 (19.23)	
	Caucasian	10 (28.57)	25 (71.43)	p<0.001
Multivitamin use	Yes	9 (36)	16 (64)	
	No	42 (65.62)	22 (34.38)	p=0.01
Sun exposure	Adequate exposure	13 (56.52)	10 (43.48)	
	Inadequate exposure	38 (57.58)	28 (42.42)	p=0.93
Vitamin D intake	Adequate intake	14 (43.75)	18 (56.25)	
	Inadequate intake	37 (64.91)	20 (35.09)	p=0.05
Calcium intake	Adequate intake	7 (50)	7 (50)	
	Inadequate intake	44 (58.67)	31 (41.33)	p=0.55
BMI	<25	32 (58.18)	23 (41.82)	
	≥25	19 (55.88)	15 (44.12)	p=0.68

study conducted during winter in Boston (USA), that despite their cohort not displaying traditional demographic characteristics associated with vitamin D deficiency, their residents had a 25% prevalence of vitamin D insufficiency. Long working hours and cold climate may have played a role, as well as the fact that many trainees spend much of their free time studying indoors. The results of Mendoza and colleagues[13] and our study confirm that not only are indoor workers residing in colder climates at risk, but also those from "sunny" climates. However, season and latitude alone cannot explain these high rates of insufficiency. Other factors influencing vitamin D levels need to be addressed. These include sun exposure, ethnicity, age, vitamin supplementation, diet, and BMI.

Haney and colleagues[10] in Portland (USA) found that sun exposure and multivitamin use were predictive of the 25(OH)D levels. While our results were not able to demonstrate that sun exposure had any statistical association with vitamin D status, we did demonstrate a significant association between multivitamin use and vitamin D status. The questionnaire also determined dietary intake of vitamin D, aside from supplementation, to be quite poor. The reason for this could be that vitamin D rich foods are not commonly consumed by South Africans.[22] Additionally, staple food fortification is not practised in South Africa, aggravating the poor dietary intake of vitamin D.

Haney and colleagues mentioned as a limitation to their study that they had a study sample that was predominantly caucasian.[10] In our study ethnicity was shown to be significantly associated with vitamin D status. The prevalence of insufficiency among anesthetists of Indian decent was 80.77%, as opposed to 70% of black African anesthetists and only 28.57% of caucasian anesthetists. This concurs with other studies that have shown darker skin pigmentation to be associated with lower 25(OH)D levels.[7,23,24] Additional reasons for varying levels of sun exposure include avoidance of the sun and cultural attire. The study of Erden and colleagues[25] in Turkey, predominantly an Islamic country, supports this notion. A previous South African study[26] mentioned diet, clothing and sun exposure as compounding factors with regard to vitamin D levels.

Our study population was relatively young, with a mean age of 31.33 years, and therefore the effect of advancing age on cutaneous vitamin D synthesis[1,23] could not be established. This makes the high prevalence of vitamin D insufficiency in our study notable, as advanced age has long been a recognised risk factor for poor vitamin D status.[17]

Owing to financial constraints, parathyroid hormone (PTH) and calcium levels were not investigated. This is a limitation of our study. Disorders of PTH and calcium may positively or negatively influence vitamin D levels. In addition, the factors influencing vitamin D levels were secondary objectives of the study and should be interpreted with caution as the sample size was not powered for these secondary objectives. Our study was conducted in winter to be able to more accurately compare our results to the published data from the majority of the studies of Vitamin D status conducted in medical personnel, which were also done during winter months. Thus seasonal variation of vitamin D levels in our cohort could not be established. Participants were only included if they had been in the department for more than one month, thus vitamin D status over a longer time period could also not be established.[27]

The strengths of our study lie in the high prevalence of vitamin D insufficiency, found among people initially not thought of as being at risk. Future research should include testing PTH and calcium levels, as well as testing vitamin D levels of anesthetists during the summer months, as deficiency during this time would be even more significant.

As an essential part of human physiology vitamin D has long been overlooked. Northern latitude countries have begun to realise its importance, but due to conventional risk stratification and a paradigm that "sunny" climates are exempt from the problem, many individuals in our study sample remain vitamin D insufficient. More importantly, the results of our study highlight the risks that may be prevalent in anesthetists in other "sunny" climates.

The extent of the risk may also be much greater than we presume. Members of the IOM, in 2016, questioned the vitamin D reference values being used by medical advisors.[28] The Endocrine Society[29] defines sufficiency for individuals at risk for deficiency as >72.5 nmol/l. The IOM defines sufficiency for free living healthy adults as >50nmol/l. From this it is clear that although the prevalence of insufficiency of 57.30% among anesthetists in our study is quite high, this could be an underestimation if anesthetists were reclassified as a population at risk.

Conclusion

Vitamin D insufficiency is associated with a myriad of health risks. Anesthetists, who work predominantly indoors, have previously been shown to have low vitamin D levels in northern hemisphere countries, with low UV indices. Our study has demonstrated that this risk is also relevant for anesthetists who work in sunny southern hemisphere climates such as South Africa.

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Conflict of interest: EK had financial support from The South African Society of Anaesthesiologists Jan Pretorius Research Fund for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work. HP, JS and SC declare no competing interests.

References

1. Holick MF. Vitamin D Deficiency. *N Engl J Med*. 2007; 357(3):266-81.
2. Braun A, Chang D, Mahadevappa K, Gibbons FK, Liu Y, Giovannucci E, et al. Association of Low Serum 25-Hydroxyvitamin D Levels and Mortality in the Critically Ill. *Crit Care Med.* 2011; 39(4):671-7.
3. Barbarawi M, Kheiri B, Zayed Y, Barbarawi O, Dhillon H, Swaid B, et al. Vitamin D Supplementation and Cardiovascular Disease Risks in More Than 83 000 Individuals in 21 Randomized Clinical Trials: A Meta-analysis. *JAMA Cardiol.* 2019; 4(8):765-776.
4. Autier P, Mullie P, Macacu A, Dragomir M, Boniol M, Coppens K, et al. Effect of vitamin D supplementation on non-skeletal disorders: a systematic review of meta-analyses and randomised trials. *Lancet Diabetes Endocrinol.* 2017 Dec; 5(12):986-1004.
5. Manson JE, Cook NR, Lee I-M, Christen W, Bassuk SS, Mora S, et al. Vitamin D Supplements and Prevention of Cancer and Cardiovascular Disease. *N Engl J Med.* 2019; 380(1):33-44.
6. Pettifor JM, Moodley GP, Hough FS, Koch H, Chen T, Lu Z, et al. The Effect of Season and Latitude on in Vitro Vitamin D Formation by Sunlight in South Africa. *S Afr Med J*. 1996 Oct; 86(10):1270-2.
7. Mithal A, Wahl DA, Bonjour JP, Burckhardt P, Dawson-Hughes B, Eisman JA, et al. Global Vitamin D Status and Determinants of Hypovitaminosis D. *Osteoporos Int.* 2009 Nov; 20(11):1807-20.
8. Lips P. Worldwide Status of Vitamin D Nutrition. *J Steroid Biochem Mol Biol.* 2010 Jul; 121(1-2):297-300.
9. Growdon AS, Camargo CA, Jr., Clark S, Hannon M, Mansbach JM. Serum 25-Hydroxyvitamin D Levels among Boston Trainee Doctors in Winter. *Nutrients.* 2012 Mar; 4(3):197-207.
10. Haney EM, Stadler D, Bliziotes MM. Vitamin D Insufficiency in Internal Medicine Residents. *Calcif Tissue Int*. 2005; 76(1):11-6.
11. Holick MF. High Prevalence of Vitamin D Inadequacy and Implications for Health. *Mayo Clin Proc*. 2006; 81(3):353-73.
12. Ardawi MS, Sibiany AM, Bakhsh TM, Qari MH, Maimani AA. High Prevalence of Vitamin D Deficiency among Healthy Saudi Arabian Men: Relationship to Bone Mineral Density, Parathyroid Hormone, Bone Turnover Markers, and Lifestyle Factors. *Osteoporos Int.* 2012; 23(2):675-86.
13. Mendoza V, Villanueva MT, Vargas G, Gonzalez B, Halabe J, Simon J, et al. Vitamin D Deficiency among Medical Residents and Its Relationship with Metabolic Indices. *Endocr Pract.* 2012; 27:1-16.
14. Binkley N, Novotny R, Krueger D, Kawahara T, Daida YG, Lensmeyer G, et al. Low Vitamin D Status Despite Abundant Sun Exposure. *J Clin Endocrinol Metab.* 2007; 92(6):2130-5.
15. World Medical Association. WMA Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Subjects. Seoul, Korea: World Medical Association, 2008.
16. Department of Health. Guidelines for Good Practice in the Conduct of Clinical Trials with Human Participants in South Africa. Pretoria, South Africa, 2006.
17. Institute of Medicine. 2011 Dietary Reference Intakes for Calcium and Vitamin D. Washington DC: Institute of Medicine, 2011.
18. Tangpricha V, Pearce EN, Chen TC, Holick MF. Vitamin D Insufficiency among Free-Living Healthy Young Adults. *Am J Med*. 2002; 112(8):659-62.
19. Sowah D, Fan X, Dennett L, Hagtvedt R, Straube S. Vitamin D Levels and Deficiency with Different Occupations: A Systematic Review. *BMC Public Health.* 2017; 17(1):519.
20. Skarphedinsdottir SJ, Sigurdsson MI, Coursin DB, Head DE, Springman SR, Wang S, et al. Vitamin D Deficiency in Anesthesia Department Caregivers at the End of Winter. *Acta Anaesthesiol Scand*. 2014; 58(7):802-6.
21. Weather Atlas. c2002-2019. Available from: https://www.weather-atlas.com/en/south-africa/johannesburg-weather-july#uv_index
22. Kruger MC, Kruger IM, Wentzel-Viljoen E, Kruger A. Urbanization of Black South African Women May Increase Risk of Low Bone Mass Due to Low Vitamin D Status, Low Calcium Intake, and High Bone Turnover. *Nutr Res.* 2011; 31(10):748-58.
23. Holick MF. The Photobiology of Vitamin D and Its Consequences for Humans. *Ann N Y Acad Sci.* 1985; 453:1-13.
24. Heaney RP. Functional Indices of Vitamin D Status and Ramifications of Vitamin D Deficiency. *Am J Clin Nutr.* 2004; 80(6 Suppl):1706S-9S.
25. Erden G, Ozdemir S, Ozturk G, Erden A, Kara D, Isik S, et al. Vitamin D Levels of Anesthesia Personnel, Office Workers and Outdoor Workers in Ankara, Turkey. *Clin Lab.* 2016; 62(5):931-7.
26. George JA, Norris SA, van Deventer HE, Pettifor JM, Crowther NJ. Effect of Adiposity, Season, Diet and Calcium or Vitamin D Supplementation on the Vitamin D Status of Healthy Urban African and Asian-Indian Adults. *Br J Nutr*. 2014; 112(4):590-9.
27. Mocanu V, Vieth R. Three-year follow-up of serum 25-hydroxyvitamin D, parathyroid hormone, and bone mineral density in nursing home residents who had received 12 months of daily bread fortification with 125 µg of vitamin D_3. *Nutr J*. 2013; 12:137.
28. Manson JE, Brannon PM, Rosen CJ, Taylor CL. Vitamin D Deficiency - Is There Really a Pandemic? *N Engl J Med*. 2016; 375(19):1817-20.
29. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, Treatment, and Prevention of Vitamin D Deficiency: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2011; 96(7):1911-30.