Published in final edited form as:

Nutrition. 2012 April ; 28(4): 362–366. doi:10.1016/j.nut.2011.08.012.

Effects of Sunlight and Diet on Vitamin D Status of Pulmonary Tuberculosis Patients in Tbilisi, Georgia

Nirali S. Desai, MD¹, Nestani Tukvadze, MD², Jennifer Frediani, MS, RD, LD^{3,4}, Maia Kipiani, MD², Eka Sanikidze, MD², Memorie M. Nichols, PA-C⁴, Gautam Hebbar, MBBS, MPH⁵, Russell R. Kempker, MD⁶, Veriko Mirtskhulava, MD, MPH², Iagor Kalandadze, MD², Shabnam Seydalkan, MD⁵, Nilay Sutaria⁷, Tai C. Chen, PhD⁷, Henry M. Blumberg, MD^{1,3,6}, Thomas R. Ziegler, MD^{3,4,5}, and Vin Tangpricha, MD, PhD^{3,5,8}

¹ Department of Medicine, Emory University School of Medicine, Atlanta, GA, USA 30322

² National Center for Tuberculosis and Lung Diseases (NCTBLD), Tbilisi, 0101, Republic of Georgia

³ Atlanta Clinical and Translational Science Institute, Emory University School of Medicine, Atlanta, GA, USA 30322

⁴ Nutrition and Health Sciences Program, Graduate Division of Biological and Biomedical Sciences, Emory University Laney Graduate School, Atlanta, GA, USA 30322

⁵ Division of Endocrinology, Metabolism and Lipids, Department of Medicine, Emory University School of Medicine, Atlanta, GA, USA 30322

⁶ Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine, Atlanta, GA, USA 30303

⁷ Section of Endocrinology, Diabetes and Nutrition, Department of Medicine, Boston University School of Medicine, Boston, MA, USA 02118

⁸ Staff Physician, Atlanta VA Medical Center, Decatur, GA USA 30033

Abstract

Vitamin D deficiency is common in tuberculosis (TB) and this may modulate immune responses.

Objective—To determine vitamin D status in patients with TB and examine sources of vitamin D in Tbilisi, Georgia.

Research Methods and Procedures—We measured plasma 25-hydroxyvitamin D (25(OH)D) and dietary vitamin D intake in pulmonary TB patients (n=85) in Tbilisi, Georgia. To determine the impact of season on vitamin D status, we tested *in vitro* conversion of 7-dehydrocholesterol (7-DHC) to previtamin D₃ after sunlight exposure.

Results—In TB subjects, mean plasma 25(OH)D concentrations were 14.5 ± 7.0 ng/mL, and vitamin D insufficiency (25(OH)D < 30 ng/mL) occurred in 97% of subjects. Dietary sources of

Corresponding Author's Address : Vin Tangpricha, MD, PhD Emory Division of Endocrinology, Metabolism & Lipids 101 Woodruff Circle – WRMB 1301 Atlanta GA 30322 Phone 404-727-7254 vin.tangpricha@emory.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Authors Contributions NSD, JF, TCC, HMB, TRZ and VT designed the experiments NSD, NT, JF, MK, ES, MMN, GH, RRR, VM, SS, NS, IK, TCC, TRZ, and VT performed the experiments NSD, JF, MMN, TCC, HMB, TRZ, VT analyzed the data NSD, JF, MMN, TCC, TRZ, VT wrote the paper IK, TCC, TRZ, HMB, and VT provided funding

vitamin D were mainly fish, eggs, and butter. Daily intake was well below recommended daily intakes in TB subjects (172 IU + 196 IU). The conversion of 7-DHC to previtamin D₃ was undetectable between October to March, and highest in June and July between 11:00 and 14:00 h.

Conclusion—Insufficient vitamin D dietary intake and limited production of vitamin D from sunlight during the majority of the year, may explain the high prevalence of vitamin D insufficiency TB patients in Tbilisi.

Keywords

cholecalciferol; 7-dehydrocholesterol; dietary intake

INTRODUCTION

Vitamin D is a seco-steroid hormone produced primarily in the skin upon exposure to UVB from the sun or obtained from limited dietary sources¹. Cutaneous production of vitamin D is the major determinant of an individual's vitamin D status¹. Vitamin D is synthesized in skin when 7-dehydrocholesterol (7-DHC) is exposed to UVB radiation and then photolysed to previtamin D₃, which then undergoes a thermally induced isomerization to vitamin D₃. After entering the bloodstream, vitamin D₃ undergoes two sequential hydroxylations to form 25-hydroxyvitamin D (25(OH)D), the major circulating form of vitamin D, followed by the hormonal form of vitamin D, 1,25-dihydroxyvitamin D (1,25(OH)²D)². Along with cutaneous production, vitamin D can be obtained from dietary sources such as fish, mushrooms, or fortified foods¹. In addition to skeletal health and calcium homeostasis, vitamin D regulates many other biological systems including the immune system³. For example, one function of vitamin D is to regulate production of cathelicidin/LL-37, an antimicrobial peptide involved in the innate immune response to *Mycobacterium tuberculosis* (TB) infection⁴. Vitamin D may have other effects on the immune system including effects on both adaptive and innate immunity^{3,5}.

There is a high prevalence of vitamin D deficiency worldwide. While the definition of vitamin D deficiency varies, most studies refer to deficiency as a plasma 25(OH)D concentration <20 ng/mL, and insufficiency as values <30 ng/mL¹. In the most recent NHANES, out of 13,369 non-institutionalized civilians in the United States from 2001-2004, 77% of the participants had vitamin D insufficiency⁶. In North America, hypovitaminosis D has been attributed to obesity, decreased outdoor activity, inadequate dietary intake of vitamin D, and sunscreen usage^{6,7,8}. In other parts of the world, residents are deficient in vitamin D due to lack of food fortification, less sunlight exposure, decreased ambulatory capability and/or institutionalization of elderly adults^{9,10}.

Given the connection between poor vitamin D status and TB infection^{11,12}, we sought to assess circulating plasma 25(OH)D concentrations and dietary vitamin D intake in pulmonary TB patients residing in Tbilisi, Republic of Georgia. We also measured the effect of sunlight on *in vitro* conversion of 7-dehydrocholesterol (the vitamin D precursor in skin) to previtamin D₃ in the environment of TB patients living in Tbilisi, Republic of Georgia.

MATERIALS AND METHODS

Study Location, Participants, and Ethics

Participants were recruited from the National Center for Tuberculosis and Lung Diseases (NCTBLD) and the Tbilisi Ftizio-Pulmonologic Center in Tbilisi as a subset of the initial subjects from a larger, ongoing double blind, randomized, controlled, prospective trial of high-dose vitamin D₃ treatment (clinicaltrials.gov identifier NCT00918086) for patients

with pulmonary TB infection. The inclusion criteria for TB patients were age above 18 years, documented new case of smear-positive pulmonary TB, ≤ 7 days of anti-TB therapy, agreement to receive anti-TB therapy in Tbilisi, and signed informed consent. The exclusion criteria for TB patients was greater than 30 days of lifetime TB therapy, current pregnancy or lactation, history of organ transplant, cancer in past 5 years (excluding non-melanoma skin cancer), seizures, hypercalcemia, hyperparathyroidism, sarcoidosis, nephrolithiasis, liver cirrhosis, serum creatinine >250 mmol/L, requirement of hemodialysis, corticosteroid use in the past 30 days, current use of cytotoxic or immunosuppressive drugs, current incarceration, inability to complete all study visits in Tbilisi.

The Institutional Review Boards from Emory University in Atlanta, USA and the NCTBLD in Tbilisi approved the study protocol. All subjects provided written informed consent for participation in the study. All data for this study was collected between November 1, 2009 and October 31, 2010.

Study Design

Evaluation of Seasonal Production of Vitamin D from Sunlight

Glass ampules containing 5 mL of synthetic 7-DHC in methanol were placed in direct sunlight for 1 hour each from 10 AM to 5 PM, monthly from November 2009 to October 2010. The investigators recorded the corresponding weather conditions. The ampule studies were completed during days where it was forecasted to be at minimum 50% to 100% sunny in attempt to capture the peak amount of vitamin D conversion during each month (www.weather.com). Two dates were studied each month and the most representative sunny day from the month was used for the analysis. The ampules were protected from light and stored in a -20 degree freezer before and after the hour-long sunlight exposure. The amount of pre-vitamin D₃ converted from 7-DHC was determined by standard high-performance liquid chromatography (HPLC) methods using previously published methods at Boston University School of Medicine, Boston, MA³.

Vitamin D status in Participants

Subjects provided demographic information on age, gender and mean daily time spent outdoors. Participants were recruited throughout the year, and each subject provided a blood specimen upon enrollment into the study. Vitamin D status was determined by plasma 25(OH)D concentrations, measured by ELISA (Immunodiagnosics, LTD, Fountain Hills, AZ) at the Vitamin D and Bone Research Laboratory, Emory University. The Laboratory participates in the international Vitamin D External Assessment Scheme (DEQAS) to ensure quality control of the plasma 25(OH)D determinations.

Assessment of Vitamin D Content in the Georgian Diet

Baseline nutritional status included body weight, measured on a digital scale (Tanita Co., Arlington Heights, Illinois), and height measured using a stadiometer, to calculate a body mass index (BMI; kg/m²). To define habitual daily vitamin D intake, one-on-one interviews were conducted by trained physicians, using a 3-day food recall questionnaire designed to capture all food and beverage intake, including staple foods and recipes common in the Georgian diet. Food models were used to accurately determine portion size of reported items. Vitamin D intake from reported intakes was quantitated by a registered dietitian (JF) at the Atlanta Clinical and Translational Science Institute Bionutrition Research Unit, Atlanta, GA using Nutrition Data System for Research software (NDS-R, version 2009, University of Minnesota, Minneapolis, MN).

Statistical Analysis

Descriptive statistics were performed for demographic information. Student's T-tests were used to determine the mean plasma 25(OH)D concentrations, daily vitamin D intake, and daily intake of specific foods containing natural vitamin D in TB subjects.

RESULTS

Seasonal Production of Vitamin D From Sunlight

The *in vitro* ampule studies demonstrated that the highest amount of previtamin D₃ production from 7-DHC occurred between May through August, and that no detectable previtamin D₃ was produced from October through March (Figure 1). The peak production of previtamin D₃ occurred between 11:00 and 14:00 h (Figure 2).

Demographics and vitamin D status in TB subjects

Demographic information of the subjects with TB is presented in Table 1. The majority of the subjects were Ethnic Georgian (91%). Mean plasma 25(OH)D concentrations were in the vitamin D deficient range (25(OH)D < 20 ng/mL) in 83% of TB subjects. Vitamin D insufficiency (25(OH)D < 30 ng/mL) was present in 97% of participants (Table 2). There were no differences in plasma 25(OH)D in the Ethnic Georgian subjects compared to the non-Ethnic Georgian subjects, (14.4 ± 7.0 vs 14.8 ± 7.0 , respectively). We did not observe higher vitamin D status in those reporting greater than 4 hours of outdoor activity daily compared to those reporting less than 1 hour of outdoor activity daily.

Dietary Vitamin D Intake

Data from the 3-day food records revealed that the most frequently ingested foods with naturally occurring vitamin D content were fish, eggs, and butter the participants. Few foods in Georgia are fortified with vitamin D. The only fortified item identified after inspection of foods at over 12 grocery stores in Tbilisi was one commercial brand of low-fat milk. The daily intake of foods containing the most vitamin D was fish (188 ± 137 g), eggs (109 ± 83 g), and butter (81 ± 54). The daily habitual intake of total vitamin D from all food sources in TB was 172 ± 196 IU (Table 2). This level of dietary vitamin D intake is considerably lower than the new 2010 Recommended Dietary Allowance (RDA) recommendations from the US Institute of Medicine (600 IU/day for adults up to age 70 and 800 IU/d for those 71 years and older)¹³.

DISCUSSION

This pilot study showed that adults with newly diagnosed pulmonary TB in Tbilisi, Georgia exhibit a very high prevalence of vitamin D deficiency and insufficiency. Dietary sources of vitamin D were quite inadequate compared to the current dietary RDA in this cohort. In addition to the limited intake of vitamin D foods, patients with pulmonary TB residing in Tbilisi, Georgia (42 ° N) had limited potential to produce vitamin D in skin during most of the year. To our knowledge, this is the first study to explore the major sources of vitamin D nutriture (sunlight and diet) in a population with pulmonary TB infection.

Several studies, including ours, have reported a high prevalence of vitamin D insufficiency in patients with TB infection^{11,14,15,16,17}. Sita-Lumsden et al reported that patients with TB had lower vitamin D status compared to healthy controls. Furthermore, they reported that patients did not experience a seasonal increase in serum 25(OH)D in the summertime as did controls, suggesting that patients with TB do not get adequate sunlight exposure either to environmental factors or due to the infection with TB itself. In addition, a majority (79%) of participants did not have an appropriate increase in serum 25(OH)D concentrations despite 3

months of vitamin D repletion. This suggests that TB patients had alterations in the vitamin D metabolism¹⁸. Given the high prevalence of vitamin D deficiency in this population, there has been interest to examine the impact of correction of vitamin D deficiency on TB outcomes; however, the data to date have yielded mixed results. This is in part due to variability in the doses, patient populations, and methodology in previously conducted trials¹⁹. Historically, dating back to the 1800's, vitamin D in the form of cod liver oil was used to treat pulmonary TB²⁰. More recently, two prospective studies have demonstrated a potential benefit of vitamin D supplementation on TB outcomes. Nursyam et al administered daily vitamin D as adjunctive therapy and found 23% greater sputum conversion compared to placebo²¹. In a randomized control trial of 126 tuberculosis patients, Martineau et al demonstrated that vitamin D as an adjunct to anti-TB drugs decreased time to sputum conversion, though only in patients with the *tt* genotype of the *taqI* vitamin D receptor polymorphism²². TB is a serious public health concern in Georgia due to poverty, lack of access to affordable healthcare, smoking, and less monitoring of drug therapy²³. Our current ongoing trial in Tbilisi, Georgia, in addition to other ongoing trials, of high dose vitamin D therapy in TB patients will shed further light on this issue.

We attempted to determine the causes of the high prevalence of vitamin D deficiency in our TB patients in Tbilisi. We found a high prevalence of vitamin D insufficiency in patients with pulmonary TB consistent with other studies at similar latitudes as Tbilisi (42 degrees N). In London (51 degrees N), Sita-Lumsden showed that only 6% TB patients had optimal serum 25(OH)D concentrations (>30 ng/mL) in contrast to 27% of healthy controls¹⁸. A few studies have been conducted to examine vitamin D status of subjects without TB infection in the proximity of Tbilisi, Georgia. In a study of 391 adults above the age of 20 in Manisa, Turkey (38 degrees N), 75% of subjects had 25(OH)D levels < 20ng/mL and 14% had levels between 20-29 ng/mL at the end of winter²⁴. In Yekaterinburg, Russia (56 degrees N), Bakhtiyarova et al reported that 161 elderly patients above the age of 65 and found that 100% of the participants exhibited vitamin D deficiency (25(OH)D < 20 ng/ml)¹⁰. In a similar study conducted in Lleida, Spain (43 degrees N), 100% of institutionalized elderly women had 25(OH)D < 30 ng/mL²⁵. Therefore, patients with TB residing in Tbilisi, Georgia, are at risk for vitamin D deficiency in part due to the high latitude in which they reside.

In addition to latitude, the amount of UVB exposure from sunlight depends on environmental and personal factors. The altitude, time of day and year, cloud cover, pollution, and solar zenith angle (the angle at which sunlight hits the Earth's surface) all affect UVB levels²⁶. Personal factors such as age²⁷, sunscreen usage²⁸, and clothing also affect UVB absorption²⁶. Most importantly, skin tone²⁹ decreases the amount of vitamin D produced by sunlight exposure. Webb et al demonstrated that the previtamin D₃ synthesis in human skin samples *in vitro* was 40-70% lower than in ampoules of 7-DHC, depending on the skin sample and color³⁰. Furthermore, Chen et al demonstrated that our *in vitro* technique best approximates vitamin D production in skin and is influenced by differences in skin tone³¹. Black patients with TB often have lower vitamin D status compared to non-Black patients³². Therefore, the differences in vitamin D status in Blacks and Whites may help explain racial disparities in TB infection.

Given the high prevalence of vitamin D deficiency in our TB patients, we examined the contribution of sunlight to vitamin D status in the region of Tbilisi, Georgia using a method that best approximates cutaneous vitamin D production in skin³¹. Webb et al showed that in Boston, the same latitude as Tbilisi, production of previtamin D₃ was highest in June and July, and no vitamin D was detectable from the months of November to February³⁰. Lu et al confirmed that more previtamin D₃ was synthesized in the summer months and that it was produced in higher amounts during the day around 12:00. They also found that cities farther

from the equator had decreased previtamin D₃ synthesis overall³³. Though cutaneous synthesis is the main source of vitamin D, our research confirms that UVB exposure adequate for vitamin D production is not available for most of the day and in winter months in Tbilisi. In our study, we did not find that vitamin D status was higher in individuals spending more time outside. This data helps explain the high rates of vitamin D deficiency in persons infected with TB living in this region and other regions that share the same latitude or higher.

In addition to sunlight, food may provide another source of vitamin D for individuals with TB infection. We found that pulmonary TB subjects had little vitamin D content in their diet, which may be due to lack of food fortification in this region or due to limited intake of foods naturally containing vitamin D. In a review of vitamin D status throughout Europe, Oveson et al showed that despite higher latitudes, participants in Sweden, Denmark, and the UK had had higher vitamin D status than in France and Italy, possibly because there was more vitamin D fortification of food in those areas⁹. Given the low levels of vitamin D intake and the high prevalence of vitamin D deficiency, Georgians would likely benefit from increased availability of vitamin D-fortified foods. A systematic review by O'Donnel in 2008 demonstrated that fortification of various foods including milk, cheese, milk powder, and orange juice, did significantly raise plasma vitamin D levels³⁴.

Limitations of our study include the lack of a control group of healthy patients. Due to the relatively small sample size of TB patients, we were not able to adequately compare plasma 25(OH)D concentrations throughout seasons of the year. Lastly, the 3-day food records may have missed intake of certain foods that participants eat regularly, as they may have not ingested it in the time period assessed.

CONCLUSIONS

Vitamin D deficiency and insufficiency are highly prevalent in patients with pulmonary TB in Tbilisi, Republic of Georgia. An evaluation of environmental and dietary factors demonstrate that UVB light between October and March is inadequate for cutaneous production of vitamin D and also that vitamin D is limited in the typical Georgian diet, respectively. Georgians, especially those with TB infection, may benefit from supplementation of vitamin D through oral preparations and fortification of food, especially during the winter months. Trials to evaluate whether vitamin D supplementation will improve health outcomes in patients with TB in this population are warranted in light of the high prevalence of vitamin D insufficiency and the potential role of vitamin D in the regulation of antimicrobial peptides involved in the innate immune response to *Mycobacterium tuberculosis* infection.

Acknowledgments

Supported in part by a grants from the Emory University Global Health Institute (TRZ, VT, HMB), National Institutes of Health grants # K23 K23AR054334 (VT), #K24 RR023356 (TRZ), #1U1RR025771 (TRZ), #1U1RR025771 (HMB, TRZ, VT), #UL RR025008 (HMB, TRZ, VT). D43TW007124 (HMB), and D43TW007124-06S109 (RRK)

REFERENCES

1. Holick MF. Vitamin D deficiency. *N Engl J Med*. 2007; 357(3):266–281. [PubMed: 17634462]
2. Holick MF, MacLaughlin JA, Clark MB, et al. Photosynthesis of previtamin D₃ in human skin and the physiologic consequences. *Science*. 1980; 210(4466):203–205. [PubMed: 6251551]
3. Kamen DL, Tangpricha V. Vitamin D and molecular actions on the immune system: modulation of innate and autoimmunity. *J Mol Med*. May. 2010; 88(5):441–50. [PubMed: 20119827]

4. Liu PT, Stenger S, Li H, et al. Toll-like receptor triggering of a vitamin D-mediated human antimicrobial response. *Science*. 2006; 311:1770–1773. [PubMed: 16497887]
5. Borges MC, Martini LA, Rogero MM. Current perspectives on vitamin D, immune system, and chronic diseases. *Nutrition*. Apr. 2011; 27(4):399–404. [PubMed: 20971616]
6. Ginde AA, Liu MC, Camargo CA Jr. Demographic differences and trends of vitamin D insufficiency in the US population, 1988–2004. *Arch Intern Med*. 2009; 169(6):626–632. [PubMed: 19307527]
7. Scragg R, Camargo CA Jr. Frequency of leisure-time physical activity and serum 25-hydroxyvitamin D levels in the US population: results from the Third National Health and Nutrition Examination Survey. *Am J Epidemiol*. 2008; 168(6):577–86. discussion 587–91. [PubMed: 18579538]
8. Wortsman J, Matsuoka LY, Chen TC, Lu Z, Holick MF. Decreased bioavailability of vitamin D in obesity. *Am J Clin Nutr*. Sep. 2000; 72(3):690–3. [PubMed: 10966885] Erratum in: *Am J Clin Nutr*. 2003 May;77(5):1342.
9. Ovesen L, Andersen R, Jakobsen J. Geographical differences in vitamin D status, with particular reference to European countries. *Proc Nutr Soc*. 2003; 62(4):813–821. [PubMed: 15018480]
10. Bakhtiyarova S, Lesnyak O, Kyznesova N, Blankenstein MA, Lips P. Vitamin D status among patients with hip fracture and elderly control subjects in Yekaterinburg, Russia. *Osteoporosis Int*. 2006; 17(3):441–446.
11. Yamshchikov AV, Kurbatova EV, Kumari M, Blumberg HM, Ziegler TR, Ray SM, Tangpricha V. Vitamin D status and antimicrobial peptide cathelicidin (LL-37) concentrations in patients with active pulmonary tuberculosis. *Am J Clin Nutr*. Sep. 2010; 92(3):603–11. [PubMed: 20610636]
12. Nnoaham KE, Clarke A. Low serum vitamin D levels and tuberculosis: a systematic review and meta-analysis. *Int J Epidemiol*. 2008; 37(1):113–119. [PubMed: 18245055]
13. Ross AC, Manson JE, Abrams SA, et al. The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. *J Clin Endocrinol Metab*. 2011; 96(1):53–58. [PubMed: 21118827]
14. Banda R, Mhemedi B, Allain TJ. Prevalence of vitamin D deficiency in adult tuberculosis patients at a central hospital in Malawi. *Int J Tuberc Lung Dis*. Mar; 15(3):408–10. [PubMed: 21333112]
15. Talat N, Perry S, Parsonnet J, Dawood G, Hussain R. Vitamin d deficiency and tuberculosis progression. *Emerg Infect Dis*. May. 2010; 16(5):853–5. [PubMed: 20409383]
16. Friis H, Range N, Pedersen ML, Mølgaard C, Changalucha J, Krarup H, Magnussen P, Søborg C, Andersen AB. Hypovitaminosis D is common among pulmonary tuberculosis patients in Tanzania but is not explained by the acute phase response. *J Nutr*. Dec. 2008; 138(12):2474–80. [PubMed: 19022975]
17. Nnoaham KE, Clarke A. Low serum vitamin D levels and tuberculosis: a systematic review and meta-analysis. *Int J Epidemiol*. Feb. 2008; 37(1):113–9. [PubMed: 18245055]
18. Sita-Lumsden A, Lapthorn G, Swaminathan R, et al. Reactivation of tuberculosis and vitamin D deficiency: the contribution of diet and exposure to sunlight. *Thorax*. Nov. 2007; 62(11):1003–7. [PubMed: 17526677]
19. Yamshchikov AV, Desai NS, Blumberg HM, Ziegler TR, Tangpricha V. Vitamin D for Treatment and Prevention of Infectious Diseases: A Systematic Review of Randomized Controlled Trials. *Endocr Pract*. 2009; 15(5):438–449. [PubMed: 19491064]
20. Williams CJB. Cod liver oil in phthisis, London. *J. Med*. 1849; 1:1–18.
21. Nursyam EW, Amin Z, Rumende CM. The effect of vitamin D as supplementary treatment in patients with moderately advanced pulmonary tuberculous lesion. *Acta Medica Indonesiana*. 2006; 38:3–5. [PubMed: 16479024]
22. Martineau AR, Timms PM, Bothamley GH, et al. High-dose vitamin D(3) during intensive-phase antimicrobial treatment of pulmonary tuberculosis: a double-blind randomised controlled trial. *Lancet*. 2011; 377(9761):242–250. [PubMed: 21215445]
23. Lomtadze N, Aspindzelashvili R, Janjgava M, et al. Prevalence and risk factors for multidrug-resistant tuberculosis in the Republic of Georgia: a population-based study. *Int J Tuberc Lung Dis*. 2009; 13(1):68–73. [PubMed: 19105881]

24. Hekimsoy Z, Dinç G, Kafesçiler S, et al. Vitamin D Status among Adults in the Aegean Region of Turkey. *BMC Public Health*. 2010; 10:782. [PubMed: 21176241]
25. Portela ML, Mónico A, Barahona A, Dupraz H, Sol Gonzales-Chaves MM, Zeni SN. Comparative 25-OH-vitamin D level in institutionalized women older than 65 years from two cities in Spain and Argentina having a similar solar radiation index. *Nutrition*. Mar. 2010; 26(3):283–9. [PubMed: 19819110]
26. Webb AR. Who, what, where and when-influences on cutaneous vitamin D synthesis. *Prog Biophys Mol Biol*. 2006; 92(1):17–25. [PubMed: 16766240]
27. MacLaughlin J, Holick MF. Aging decreases the capacity of human skin to produce vitamin D3. *J Clin Invest*. Oct. 1985; 76(4):1536–1538. [PubMed: 2997282]
28. Matsuoka LY, Ide L, Wortsman J, MacLaughlin JA, Holick MF. Sunscreens suppress cutaneous vitamin D3 synthesis. *J Clin Endocrinol Metab*. 1987; 64(6):1165–1168. [PubMed: 3033008]
29. Holick MF, MacLaughlin JA, Doppelt SH. Regulation of cutaneous previtamin D3 photosynthesis in man: skin pigment is not an essential regulator. *Science*. 1981; 211(4482):590–593. [PubMed: 6256855]
30. Webb AR, Kline L, Holick MF. Influence of season and latitude on the cutaneous synthesis of vitamin D3: exposure to winter sunlight in Boston and Edmonton will not promote vitamin D3 synthesis in human skin. *J Clin Endocrinol Metab*. Aug. 1988; 67(2):373–8. [PubMed: 2839537]
31. Chen TC, Chimeh F, Lu Z, Mathieu J, Person KS, Zhang A, Kohn N, Martinello S, Berkowitz R, Holick MF. Factors that influence the cutaneous synthesis and dietary sources of vitamin D. *Arch Biochem Biophys*. Apr 15. 2007; 460(2):213–7. [PubMed: 17254541]
32. O'Donnell MR, Chamblee S, von Reyn CF, Ellerbrock TV, Johnson J, Marsh BJ, et al. Racial disparities in primary and reactivation tuberculosis in a rural community in the southeastern United States. *Int J Tuberc Lung Dis*. Jun. 2010; 14(6):733–40. [PubMed: 20487612]
33. Lu, Z.; Chen, TC.; Kline, L., et al. Photosynthesis of previtamin D3 in cities around the world.. In: Holick, MF.; Kligman, A., editors. *Biologic effects of light. Symposium proceedings*. Walter De Gruyter & Company; Berlin: October 13-15. 1991 1992 p. 28-51.
34. O'Donnell S, Cranney A, Horsley T, et al. Efficacy of food fortification on serum 25-hydroxyvitamin D concentrations: systematic review. *Am J Clin Nutr*. 2008; 88(6):1528–1534. [PubMed: 19064512]

Figure 1. Percent conversion of 7-dehydrocholesterol (7-DHC) to previtamin D₃ by month of year in Tbilisi, Georgia

Ampules containing 7-DHC were placed in direct sunlight hourly from 10:00-17:00 h once a month for one year in Tbilisi, Georgia. The percent conversion to previtamin D₃ was analyzed using HPLC. The mid-day conversion rates (12:00-13:00 h) are presented for each month. The most efficient conversion of 7-DHC to previtamin D₃ occurred between May to August. There was no detectable production of previtamin D₃ from September to March.

Figure 2. Percent conversion of 7-dehydrocholesterol (7-DHC) to previtamin D₃ by time of day in Tbilisi, Republic of Georgia

Ampules containing 7-DHC were placed in direct sunlight hourly from 10:00-17:00 h on one sunny day each month for one year in Tbilisi, Republic of Georgia. The percent conversion to previtamin D₃ was analyzed using HPLC. The most previtamin D₃ was produced from 12:00 to 13:00h with no conversion seen from September through March.

Table 1

Demographic information of TB cases

	TB cases N=85
Age , mean (SD)	33 (12)
Gender , n (%)	
Male	53 (62)
BMI (kg/m²) , mean (SD)	21.0 (3.7)
Ethnicity , n (%)	
Ethnic Georgian	77 (91)
Azeri	1 (1)
Armenian	3 (4)
Russian	2 (2)
Ossetian	1 (1)
Other	1 (1)
Daily Time Outdoors , n (%)	
<30 min	3 (4)
30 min-1 hour	17 (20)
1-2 hours	20 (24)
2-4 hours	18 (21)
> 4 hours	27 (32)

Table 2

Vitamin D Intake and Vitamin D Status of TB cases

	TB cases N=85
Daily Vitamin D Intake, IU (SD)	172 (196)
Plasma 25(OH)D, ng/mL (SD)	14.4 (7.0)
Vitamin D deficiency (25(OH)D < 20 ng/mL) (%)	83%
Vitamin D insufficiency (25(OH)D < 30 ng/mL) (%)	97%