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Medicaid Participants in Long-Term Care at Increased Risk of Insufficient 25-Hydroxyvitamin D [25 (OH)D] Serum Levels

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Received: August 19, 2020; **Published:** January 30, 2021

DOI: 10.31080/ecnu.2021.16.00906

Abstract

Objectives: There is no agreement among health organization on 25-hydroxyvitamin D [25 (OH)D] serum cut-points used to define vitamin D insufficiency. While the U.S. Endocrine Society defines levels < 30 ng/ml as insufficient, the National Academy of Science deems serum levels < 20 ng/ml as insufficient. To determine if the < 30 ng/ml level overclassifies risk, we examined baseline characteristics and health-related conditions associated with serum levels < 30 ng/ml in older adults living in long-term care (LTC) communities.

Design and Setting: This cross-sectional study recruited residents from LTC communities in Austin, Texas. Onsite medical records were used to collect a one-year medical history and a one-time blood draw was obtained.

Participants: 173 older adults > 65 years old in LTC communities.

Measurements: Sociodemographic, lifestyle factors, diagnoses, medications, vitamin/mineral supplementation, anthropometric and biochemical measurements (including 25 (OH)D).

Methods: Baseline characteristics, mean 25 (OH)D serum levels, prevalence of insufficiency, and supplementation rates were determined through descriptive statistics. T-test, Chi-square, or ANOVA determined differences in prevalence of vitamin D insufficiency and in mean serum levels across health-related conditions. Multiple logistic regression described the relationship between health-related conditions and insufficient serum levels.

Results: Prevalence of vitamin D insufficiency (defined as < 30 ng/ml) was 56%, despite a mean supplementation rate of 58.5%. When compared to private pay individuals, Medicaid participants had significantly higher prevalence of insufficiency (48% vs 58%, p = 0.021) and were 3.26 times more to have insufficient 25 (OH)D serum levels ([OR (95%CIs)] (3.26, 1.25 - 8.48). Across health conditions, individuals diagnosed with dementia (p = 0.013), depression (p = 0.027), Alzheimer's (p = 0.016) and autoimmune conditions (p = 0.05) had significantly lower mean 25 (OH)D serum levels, compared to those not diagnosed; prevalence of insufficiency was between 51% and 70% in people with any of these conditions. Participants prescribed sertraline had lower serum levels (p = 0.009) compared to those not prescribed and had higher prevalence of insufficiency (71% vs 51%). Diagnosis of rheumatoid arthritis (p = 0.001), psoriasis (p = 0.002, irritable bowel syndrome (p = 0.002), and those prescribed sertraline (p = 0.002) were associated with lower 25 (OH)D serum levels. Health-related factors associated with insufficiency included, prescribed sertraline (2.48, 1.06-5.82), Alzheimer's (3.04, 1.26 - 7.35), depression (3.02, 1.06 - 8.62) and supplementation < 800 IU per day (OR 9.20 1.67 - 20.2).

Conclusion: Despite no significant difference in supplementation rates the prevalence of vitamin D insufficiency was greater in Medicaid participant, those diagnosed with dementia, depression, Alzheimer's, autoimmune diseases, and those taking antidepressants including Sertraline. Non-skeletal health conditions associated with serum levels < 20 ng/ml, were found to also be associated with serum levels < 30 ng/ml. These health conditions include autoimmune disease, depression, dementia and Alzheimer's.

Keywords: *Vitamin D; 25-Hydroxyvitamin D; Long-Term Care; Older Adults; Skilled-Nursing*

Introduction

Vitamin D deficiency and insufficiency is a worldwide health epidemic affecting both developing and developed countries [1]. Over one billion individuals are estimated to have inadequate serum levels; however, the World Health Organization has yet to issue a public health emergency [2]. Individuals living in high latitudes, veiled women, habitual sunscreen users, dark-skin individuals, infants, children, and older adults (> 65 years), specifically adults living in long-term care (LTC) communities, are at increased risk for deficiency [3].

Maintaining optimal vitamin D serum levels in older adults is particularly important because of its direct role in bone mineralization, cardiovascular and muscle health, and immunity [4-6].

Prevalence of deficiency among older adults living in the general public is greater than 45%; this rises to 70-94% among adults living in LTC communities [7-9]. Older adults in LTC are at increased risk for deficiency because of limited sun (UV-B light) exposure, physiological changes in the skin that decreases synthesis of vitamin D upon UV-B light exposure, difficulty meeting dietary requirements and lack of supplementation [10,11].

Vitamin D deficiency is an acknowledged risk factor for muscle weakness, osteoporosis, and fractures [12]. An association between vitamin D deficiency and cognitive decline, Alzheimer's disease, cancer, autoimmune diseases, diabetes and increased mortality rates has been found in several studies [13-15]. Preventing and/or correcting vitamin D deficiency is starting to be recognized as an important component in maintaining overall health and some LTC communities are using vitamin D supplementation as an indicator of care when evaluating quality assurance performance [16].

Vitamin D status is assessed by measuring serum 25-hydroxyvitamin D [25 (OH)D]. Experts worldwide agree that vitamin D deficiency cutoff values should be determined by "health-based reference values" the threshold at which health is affected [17,18]. Currently, the threshold for vitamin D deficiency in older adults is based on 25 (OH)D serum levels that affect bone health [19]. However, there is no consensus among researchers, regulatory health agencies, or international health organizations on optimal 25 (OH)D serum levels, vitamin D deficiency reference values, supplementation rates, or clinical practice guidelines for older adults [20,21].

There is general consensus that optimal serum levels > 30 ng/ml are needed to maintain bone health and serum levels associated with deficiency is < 12 ng/ml, but serum levels between these 12 and 30 ng/ml tend to be a "grey area" [12,22,23]. Many health organizations, including the Health and Medicine Division (HMD) of the National Academy of Science, considers ≤ 12 and < 20 ng/ml as insufficient serum levels but regards this range as asymptomatic with the exception of the association with reduced bone density [23]. The U.S. Endocrine Society defines serum 25 (OH)D levels of < 30 ng/ml as insufficient and recognizes that serum levels are possibly associated with non-skeletal health conditions [12]. As with 25 (OH)D serum levels there is no consensus among health organizations regarding the amount of vitamin D supplementation required to maintain health [20]. Regardless of the serum setpoint used to define deficiency and consensus for supplementation, studies consistently show high vitamin D deficiency prevalence in those living in LTC communities. There is consensus that older adults living in LTC require supplementation [24,25], although the prevalence of supplementation in TLC is inconsistent and varies between 5 and 50% [24,26].

Many studies have examined vitamin D deficiency and/or insufficiency, prevalence, and associated risk factors in LTC using the HMD's reference range and define deficiency and/or insufficiency as < 20 ng/ml; however, few studies have examined the prevalence and risk factors associated with insufficient serum levels (< 30 ng/ml) [2,9,27-29].

Aim of the Study

The aims of this study were to investigate the prevalence of 25-hydroxyvitamin D [25 (OH)D] insufficiency; compare 25 (OH)D serum levels and supplementation rates across baseline characteristics and health-related conditions; and identify factors associated with insufficient serum levels in older adults living in LTC communities.

Methods

Study design and population

All older adults (> 65 yr.) in Assisted Living (AL) and/or Skilled Nursing Facilities (SNF) from five LTC communities in Central, Texas were eligible to participate in this cross-sectional study. There were no exclusion criteria for vitamin D supplementation or 25 (OH)D serum levels. Written informed consent was obtained from all participants' legal proxies along with assent from those with the mental capacity to understand the presented material. Participants could opt out of any part of the study, including the blood draw. The study protocol was approved by the Institutional Review Board, University of Texas at Austin (2018-03-0030).

Data collection

Up to a one-year medical history was obtained from on-site medical records by trained data collectors using double-blinded data abstraction protocol [30,31]. Data were collected throughout May through August of 2018, when 25 (OH)D serum levels are expected to be the highest [3,12].

Information abstracted from medical records included sociodemographic (age, gender, marital status, level of care, and payer source), lifestyle factors (history/current use of tobacco and alcohol), medical diagnoses, and current medications along with dosage and start dates. Nutritional status was determined through a mini-nutritional assessment score (MNA® Nestle-Strasse Toulouse, France) and body mass index (BMI-kg/m^2) [32]. Current and/or history of dietary supplementation along with dosage, start and/or discontinue date was also obtained along with biochemical measurements (complete blood count, comprehensive metabolic panel, c-reactive protein (CRP) and 25 (OH)D).

Vitamin D supplementation was defined as a supplement containing ≥ 200 IU of vitamin D_2 or D_3, which included single-ingredient vitamin D supplements, vitamin D with calcium, and multivitamins. To determine the amount of vitamin D from multivitamins, the Director of Nursing from each community provided the house multivitamin formulary and/or brand given to participants. Medications were also categorized according to the Food and Drug Administration's USP (U.S. Pharmacopeia) Therapeutic Category and Pharmacologic Classification Guidelines (e.g. antidepressants, diuretics) [33].

Communities provided spring/summer 2018 four-week cycle menus along with the corresponding serving sizes and nutritional analyses; however, vitamin D totals were not included in analyses. The estimated average of vitamin D provided in meals per day was calculated using the USDA Nutrient Composition Database by a trained LTC-Registered Dietitian Nutritionist [34]. Specific recipes were not provided; however, serving sizes were provided and included in the analyses. To ensure the calculated analysis was credible, the macro and micro-nutrients of the calculated analysis was compared to the nutritional analysis provided by each LTC community. Oral nutritional supplementation (i.e. calorie/protein drink) was documented and the amount of vitamin D provided was included in the daily nutrient totals for each participant.

Measurements

A physician's order was obtained for all biochemical measurements, and laboratory analysis was obtained for each participant during the data collection time period. To ensure regulatory compliance with the Center for Medicare and Medicaid Services (CMS) and Texas Department of Health and Human Services, a full-service mobile diagnostic phlebotomy and laboratory company that was both Joint Commission Accredited and CLIA-88 certified (Clinical Laboratory Improvement Amendments) through CMS was contracted to collect blood samples and analyze serum concentration levels (Schryver Medical Denver, Colorado).

For statistical analysis, the U.S. Endocrine Society clinical practice guidelines were used to define serum 25 (OH)D levels as > 30 ng/ml as adequate and < 30 ng/ml as insufficient [12].

Statistical analysis

Descriptive analyses determined mean serum 25 (OH)D levels, prevalence of vitamin D adequacy (> 30 ng/mL) and insufficiently (< 30 ng/ml), supplementation rates and baseline characteristics within the population. Depending on the variable (continuous, categorical, or more than two groups) t-test, chi-square, or ANOVA were used to determine mean differences between 25 (OH)D serum levels and supplementation rates for gender, race, medical diagnosis, level of care, medications, payer source, and supplementation rates below and above the DRI for adults > 70 years old (800 IU/day), along with other health-related variables. Continuous variables are reported as means ± standard deviations and categorical variables as percentages. Factorial analysis of covariance (ANCOVA) compared serum 25

(OH)D levels between supplemented and non-supplemented groups, medical diagnoses affecting more than 15% of the population, the twelve most prescribed USP Therapeutic and Pharmacologic classifications, medications prescribed to 20% or more of the population, and other health-related risk factors.

Analyses controlled for the following covariates: amount of vitamin D provided from meals, total vitamin D supplementation rate per day, age, gender, race, BMI, MNA® score, diet order, renal and liver disease, and medications inhibiting or interfering with vitamin D metabolism. Multiple logistic regression was used to find the best fitting model that describes the relationship between insufficient (< 30 ng/ml) 25 (OH)D serum level across supplemented and non-supplemented groups, and health-related conditions while controlling for the above covariates. P-values were not corrected for multiple hypothesis testing, so uncorrected p-values of < 0.05 were considered significant. Stata v14 was used to perform statistical analysis (StataCorp, College Station, Texas).

Results

Levels of care provided by the LTC communities consisted of assisted living (n = 1), skilled nursing facilities (n = 2), or a combination of the two (n = 2). All LTC communities accepted private pay and Medicare payer sources, with two of the five also accepting Medicaid participants. Four communities were not-for-profit organizations.

Of the 180 participants recruited, 173 provided blood samples (four refused blood draws and three were deceased). The mean age was 83.0 years, with an average BMI of 26.3. As seen in table 1, 107 (61.2%) were female, 159 (89%) were Caucasian, and 62 (35%) resided in assisted living, while 111 (65%) were in a skilled nursing facility. Payer source distribution was private pay (n = 95, 55%), Medicare (n = 15, 9%), and Medicaid (n = 63, 36%).

Parameters	(n, %)	Mean Supplement rate/day (IU)† (n, %)	p-value	Supplement (%)	Mean serum levels (ng/mL)‡ (n, %)	p-value	Insufficient < 30 ng/mL (%)
Study Population	173 (100)	1190 (152.18)		58.4	32.38 (1.23)		56.2
*Meet DRI	77 (44.5)	2500 (278.27)		43.2	41.02 (2.07)		30
Did NOT meet DRI	96 (55.5)	121 (19.25)	0.0000	56.8	25.45 (1.02)	0.0000	70
Gender							
Female	107 (61.2)	1200 (220.94)		31.2	32.71 (18.3)		53
Male	66 (38.8)	1184 (181.76)	0.958	43.7	31.83 (12.3)	0.365	58
Race							
Caucasian	159 (89)	1235 (253.75)		60	32.89 (16.56)	0.724	55
Non-Caucasian	19 (11)	840 (164.32)	0.929	46	28.48 (16.24)		53
Level of Care							
AL	62 (35)	1300 (336.51)		64	35.45 (20.35)		48
SNF	111 (65)	1100 (145.05)	0.501	55	30.66 (13.17)	0.062	59
Payer Source							
Private	95 (55)	1134 (153.25)		56	36.00 (18.31)	0.324	48
Medicare	15 (9)	613 (103.09)		33	28.23 (12.29)		73
Medicaid	63 (36)	1493 (233.63)	0.238	66	30.40 (13.39)	0.021	58
*DRI = 800 IU/day							

Table 1: *Population characteristics- Mean 25 (OH)D serum levels, supplementation rate, and prevalence of insufficiency. NOT meeting RDA includes participants who were not supplemented and received meals/snacks that did not meet DRI. †Supplementation continuous variables reported as means ± standard error. ‡Serum continuous variables reported as means ± standard deviation. P-values obtained by t-test, Chi square, and ANOVA depending on variable. DRI: Dietary Reference Intake; AL: Assisted Living; SNF: Skilled Nursing Facility.*

As seen in table 1, the mean ± SD of 25 (OH)D serum level was 32.38 ± 1.23 IU with 56.2% having insufficient serum levels (43.8% adequate). Mean supplementation rate per day ± SE was 1190 ± 152 IU with 58.4% receiving a daily form of vitamin D supplementation. However, of those supplemented 56.8% dose rate failed to meet the DRI for vitamin D (800 IU/day) (2500 vs 121 IU, $p < 0.000$) and had a mean serum level of 25.45 ± 1.02 (41.02 vs 25.45 ng/dl, $p < 0.000$). Insufficient serum levels were seen in 48% of participants with private pay and 58% with Medicaid (mean serum level 36 ± 18.3 vs 30.4 ± 13.4 ng/ml, $p = 0.021$).

Table 2 shows the prevalence of health-related conditions and prevalence of 25 (OH)D insufficiency and supplementation rates within disease conditions and health-related risk factors. One hundred and fourteen (66%) participants had a diagnosis of non-Alzheimer's dementia, 97 (56%) with depression, 34 (20%) with Alzheimer's, 120 (69%) had hyperlipidemia, and 74 (43%) had congestive heart failure. Ninety (52%) percent were prescribed an antidepressant with 20% taking sertraline (i.e. Zoloft), and 88 (51%) were on a medication that interfered or inhibited vitamin D metabolism.

Health-Related Conditions	(n, %)	Mean Supplement rate /day (IU)†	p-value	Supplement (n, %)	Mean serum levels (ng/mL)‡	p-value	Insufficient < 30 ng/mL (n, %)
Medical Diagnosis							
DX of Dementia (non-alz)							
Yes	114 (66)	1097 (182.23)		63 (55.3)	30.11 (14.67)		67 (59.0)
No	59 (34)	1363 (273.93)	0.4062	41 (69.5)	36.75 (18.22)	0.013	29 (49.0)
DX of Depression							
Yes	97 (56)	1090 (149.71)		58 (60)	29.97 (13.65)		57 (60.0)
No	76 (44)	1315 (287.68)	0.4629	46 (60.5)	35.45 (18.66)	0.027	39 (51.3)
DX of Alzheimer's							
Yes	34 (20)	756 (200.44)		18 (53)	26.39 (12.68)		24 (70.5)
No	139 (80)	1293 (181.27)	0.1662	86 (62)	33.84 (16.69)	0.016	72 (51.8)
DX Nervous Sys. Disorder							
Yes	52 (30)	1070 (192.36)		38 (73.0)	31.94 (13.9)		28 (53.8)
No	121 (70)	1477 (230.41)	0.2258	66 (54.5)	32.56 (17.15)	0.818	68 (56.0)
DX of Hypertension							
Yes	138 (80)	1042 (120.88)		84 (60.8)	32.67 (16.91)		70 (50.7)
No	35 (20)	1026 (252.20)	0.9519	20 (57)	31.35 (13.83)	0.65	26 (74.0)
DX of Hyperlipidemia							
Yes	120 (69)	1280 (179.19)		78 (65)	33.59 (17.02)		58 (48.3)
No	53 (31)	988 (286.96)	0.3766	26 (49)	29.62 (14.04)	0.138	38 (71.6)
DX of CHF							
Yes	74 (43)	1380 (303.55)		47 (63.5)	34.345 (18.75)		33 (44.6)
No	99 (57)	1055 (142.63)	0.2976	57 (57.5)	30.82 (13.94)	0.149	63 (63.6)
DX of Autoimmune Disorder							
Yes	27 (16)	1600 (407.45)		16 (59.2)	30.40 (14.87)		17 (62.9)

No	146 (84)	1100 (163.71)	0.2254	88 (60)	32.74 (16.48)	0.05	79 (54.0)
DX of IBS							
Yes	10 (6)	1380 (336.770		5 (50.0)	27.5 (16.26)		7 (70.0)
No	163 (90)	1135 (157.10)	0.7618	99 (60.7)	32.67 (16.48)	0.333	89 (54.6)
DX of Liver Disease							
Yes	8 (5)	850 (235.31)		4 (50.0)	21.93 (16.81)		7 (87.5)
No	165 (95)	1200 (156.99)	0.6289	100 (60.6)	32.88 (16.07)	0.061	89 (53.9)
DX of Renal Disease							
Yes	55 (32)	1500 (251.05)		35 (63.6)	32.52 (12.28)		24 (43.6)
No	118 (68)	1060 (189.61)	0.213	69 (58.4)	32.31 (17.82)	0.094	72 (61.0)
Medications							
Prescribed Antidepressant							
Yes	90 (52)	1058 (156.28)		52 (57.7)	30.1 (14.86)		51 (56.7)
No	83 (48)	1332 (267.18)	0.3696	52 (62.6)	34.84 (17.34)	0.054	45 (54.2)
Prescribed Sertraline (Zoloft)							
Yes	35 (20)	1269 (303.18)		18 (51.4)	26.06 (15.30)		25 (71.4)
No	138 (80)	1171 (174.71)	0.7987	86 (62.3)	33.98 (16.11)	0.009	71 (51.4)
Prescribed Bisphosphate							
Yes	5 (3)	2150 (555.08)		5 (100)	54.52 (38.86)		2 (40.0)
No	168 (97)	1160 (155.41)	0.283	99 (59)	31.72 (14.83)	0.0018	99 (58.9)
Medication inhibiting Vit D							
Yes	88 (51)	1280 (261.19)		55 (62.5)	34.16 (19.13)		45 (51.1)
No	85 (49)	1100 (160.33)	0.5555	49 (57.6)	30.65 (12.68)	0.155	51 (60.0)
Therapeutic Diet							
On a NAS diet							
Yes	15 (9)	2000 (573.43)		11 (73.3)	38.14 (17.38)		4 (26.7)
No	158 (91)	1115 (156.84)	0.1025	93 (58.9)	31.83 (16.06)	0.15	92 (58.2)

Table 2: *Health-related conditions-Prevalence of 25 (OH)D insufficiency with mean serum levels and supplementation rate. Adjusted for Age, BMI, amount of vitamin D provided from meals, total vitamin D supplementation rate per day, gender, race, mini-nutritional assessment (MNA® score), diet order, renal and liver disease and medications interfering vitamin D metabolism.*

†Supplementation continuous variables reported as means ± standard error.

‡Serum continuous variables reported as means ± standard deviation.

T-test used to determine p-values for continuous variables.

DX: Diagnosis; NAS Diet: No Added Salt; IBS: Irritable Bowel Syndrome; CHF: Congestive Heart Failure.

Of those diagnosed with non-Alzheimer's dementia, 59% were insufficient and had lower serum levels than those not diagnosed (30.11 ± 14.67 vs 36.75 ± 18.22, p = 0.013). Sixty percent of those diagnosed with depression were insufficient and had lower mean serum

levels (29.97 ± 13.65 vs. 35.45 ± 18.66, p = 0.027). Of those diagnose with Alzheimer's disease, 70.5% were insufficient and had lower mean serum levels compared to those not diagnosed (26.39 ± 12.68 vs 33.84 ± 16.69, p = 0.016). Those diagnosed with an autoimmune condition had lower serum levels compared to those not diagnosed (30.40 ± 14.87 vs 32.74 ± 14.87, p = 0.05); and 63% had insufficient serum levels.

Participants prescribed sertraline had lower serum levels compared to those not (26.06 ± 15.30 vs 33.98 ± 16.11, p = 0.009); and 71% had insufficient serum levels. Participants prescribed a bisphosphate had higher serum levels compared to those who were not (54.52 ± 38.86 vs 31.72 ± 14.83, p = 0.002).

Table 3 shows the associations of baseline characteristics and the health-related conditions with 25 (OH)D serum levels. The model in table 3 included baseline characteristics, all medical diagnoses affecting at least 15% or more of the sample population and top twelve prescribed therapeutic and pharmacologic classification; however only significant independent variables with controls shown. Diagnosis of rheumatoid arthritis (p = 0.001), psoriasis (p = 0.002), disease of the nervous system (p = 0.04), irritable bowel syndrome (p = 0.002), "other" autoimmune diseases (p = 0.019), and sertraline (p = 0.002) were associated with lowering 25 (OH)D serum levels. Amount of vitamin D supplemented (p > 0.000), C-reactive protein levels (p > 0.000), medication that inhibit vitamin D and anticonvulsants (p = 0.022 and p = 0.047, respectively) and no added salt diet (p = 0.038) were all associated with increasing serum levels. Medical diagnosis affecting 50% of more population and top twelve therapeutic and pharmacologic classification.

Health-related risk factors	Coef.	p-value	95% Conf. Interval	
Baseline Characteristics				
Age	0.094654	0.563	-0.23007	0.419379
Race	3.242743	0.667	-11.6903	18.17574
Gender	1.376155	0.655	-4.72636	7.478668
BMI	0.441188	0.13	-0.13312	1.015501
MNA® score	-0.09614	0.904	-1.6748	1.482514
Total Vit D supplement/day	0.00686	0.000	0.004547	0.009173
Vit D provided in meals/day	-0.00933	0.494	-0.03639	0.017721
Medical Diagnosis				
Liver Disease	-10.4354	0.169	-25.4106	4.539758
Renal Disease	1.789555	0.573	-4.50539	8.084501
Dx of Autoimmune Disorder	-45.4191	0.002	-73.793	-17.0452
Rheumatoid	-40.2298	0.001	-62.9199	-17.5398
Psoriasis	-44.6287	0.002	-71.6749	-17.5825
IBS	-34.9831	0.002	-56.592	-13.3743
Nervous System Disorder	-6.34314	0.04	-12.3809	-0.30533
Therapeutic Diets				
NCS diet	-3.67855	0.400	-12.3454	4.988286
NAS diet	10.97954	0.038	0.645021	21.31405
Heart Healthy diet	-11.2907	0.315	-33.5166	10.9352
Medications				
Bisphosphate Medication	15.77578	0.047	0.190788	31.36078
Anticonvulsant Medication	7.2941	0.022	1.085242	13.50296
Medicine inhibit Vit D	5.634813	0.047	0.065469	11.20416
Sertraline (Zoloft)	-12.2686	0.002	-20.0712	-4.46607
Biochemical Measurements				
C-reactive protein	0.808601	0.000	0.396317	1.220885

Table 3: *Health-related risk factors predicting serum 25 (OH)D levels.*
ANCOVA with independent variables predicting serum 25 (OH)D levels.
Only significant health-related risk factors (independent variables) with covariates shown.
Model included baseline characteristics and medical diagnoses affecting at least 15% or more of sample population and top twelve prescribed therapeutic and pharmacologic classification. BMI: Body Mass Index; NCS Diet: No Concentrated Sweets; NAS Diet: No Added Salt; Dx: Diagnosis; IBS: Irritable Bowel Syndrome.

The following variables were significant determinants of insufficient 25 (OH)D serum levels (Table 4): Medicaid as a payer source (odds ratio (OR) 3.26; CL: 1.25, 8.48; p = 0.015), sertraline (OR 2.48; CL: 1.06 - 5.82; p = 0.037), Alzheimer's Disease (OR 3.04; CL: 1.26 - 7.35; p = 0.014), Depression (OR 3.02; CL: 1.06 - 8.62, p = 0.038) and supplementation less than the DRI (OR 9.20; CL: 1.67 - 20.2, p > 0.001).

Health-related risk factors	Odds Ratio (95% Conf. Interval)	p-value
Baseline Characteristics		
Age	1.01 (0.94 - 1.07)	0.798
BMI	0.93 (0.10 - 1.07)	0.216
Gender	1.36 (0.44 - 4.25)	0.595
Race	1.01 (0.45 - 2.28)	0.98
MNA-Score	1.20 (0.9 - 1.58)	0.177
Total Supplement/Intake per day	0.997 (0.990 - 0.996)	0.000
Payer Source- Medicaid	3.26 (1.25 - 8.48)	0.001
Supplemented > 800 ID/day	9.20 (1.67 - 20.29)	0.001
Therapeutic Diets		
NAS diet	0.37 (0.08 - 1.50)	0.159
NCS diet	1.91 (0.53 - 6.89)	0.321
Medical Diagnosis		
Dx of Depression	3.02 (1.06 - 8.62)	0.038
Dx of Alzheimer's Disease	3.04 (1.26 - 7.35)	0.014
DX of Liver Disease	5.26 (0.24 - 117.3)	0.294
Dx of Kidney Disease	0.26 (0.07 - 0.93)	0.038
Medications		
Bisphosphate Medication	1.45 (0.13 - 17.02)	0.763
Medicine inhibit Vit D	0.68 (0.25 - 1.91)	0.462
Sertraline (Zoloft)	2.48 (1.06 - 5.82)	0.037

Table 4: *Significant health-related risk factors associated with insufficient 25 (OH)D serum levels. Logistic Regression used it determine p-value.*

Adjusted for Age, BMI, amount of vitamin D provided from meals, total vitamin D supplementation rate per day, gender, race, MNA® score, diet order, renal and liver disease, and medications inhibition or interfering vitamin D metabolism.

BMI: Body Mass Index; NCS Diet: No Concentrated Sweets; NAS Diet: No Added Salt; Dx: Diagnosis; MNA: Mini-Nutritional Assessment.

Discussion

The results from this study show that, during a Texas summer, prevalence of vitamin D insufficiency in older adults living in LTC communities is high, with more than 56% of participants having serum 25 (OH)D levels < 30 ng/ml. These finding are similar to the Health ABC study by Shea., *et al*. that found 69% of community-dwelling older adults had insufficient (< 30 ng/ml) serum levels [35]. Arnljots., *et al*. also found high prevalence (90%) of insufficient serum levels in Swedish nursing home residents [9].

The demographic characteristics of the sample population are consistent with the U.S. Census Bureau's 2013 - 2017 American Community Survey (ACS) which produces population, demographic, and housing estimates for the nation. ACS estimates that 64.5% of nationally "institutionalized" adults (> 65 years) are women, with a mean age of 73.2 years old, and 83.5% are white. In our study, race was categorized into Caucasian and non-Caucasian due to the limited number of minorities participates. Medicaid is the largest funding source for LTC in the U.S. with CMS estimating that 62% of those residing in LTC depend on Medicaid to cover the cost; however, our sample popula-

tion consisted of 35% Medicaid [36]. In this study only two of the five LTC communities accept Medicaid and explains why our sample population was below the national average.

Baseline characteristics did not show any statistical significance for supplementation, serum levels, and percent of insufficiency, with the exception of Medicaid participants and individuals not meeting the DRI for vitamin D. To the best of our knowledge, this study is the first to determine that Medicaid participants had statistically significant lower mean serum levels and higher insufficiency rates of 58% vs. 48% compared to private pay individuals. Adjusted logistic regression showed that payer source was a significant determinant of insufficient 25 (OH)D serum levels. Medicaid residents were 3.26 times more likely than private pay participants to have insufficient 25 (OH)D serum levels. This find could be related to the below-cost Medicaid reimbursement rate for LTC in Texas. LTC communities caring for Medicaid residents are required to cover all the cost associated with total medical, phycological, and social needs, in addition to providing social services, room and board, over-the-counter medications/supplements, medical supplies and equipment, and any personal items needed for each resident [37]. According to the Texas Health Care Association "communities across Texas struggle to meet the most rigorous industry regulations in the nation, the state continues to reimburse providers nearly $27 per day less than the cost of care, per Medicaid resident, according to the latest Medicaid Cost Report Data." With reimbursement rates below cost levels communities have to cut all non-essential expenses to meet basic operational cost which ultimately affects the quality of medical care [38].

As expected, not meeting the DRI (800 IU/day) through supplementation or meals was also a strong determinant of 25 (OH)D serum levels. Vitamin D supplementation resulted in an increase of .00684 of 25 (OH)D serum levels for every additional IU given in this population. In more realistic terms, serum levels increase 6.84 points for every 1000 IU/day. These finding are consistent with a study by Veleva., *et al*. that found supplementation of 5600 IU vitamin D per week (800 IU per day) brought 80% of participants to optimal serum levels (> 30 ng/ml) [16].

This study also showed that over 58% of participants received at least one form of vitamin D supplementation, which is higher than the 5 - 50% estimated supplementation rate found in the literature [24,26,39]. These finding confirm that of a 2016 study that determined 54.6% of LTC general practitioners systematically prescribed a vitamin D supplement to their patients [24]. Despite high rates of supplementation, 56% of participants had insufficient serum 25 (OH)D serum levels (< 30 ng/ml). Upon examination of the supplemented dosage rates, 56.8% of the study's population failed to meet the DRI of 800 IU per day, which likely contributed to the low 25 (OH)D levels. Because of limited food sources, decreased UV-B exposure, and menus not providing adequate vitamin D, these results support the growing opinion that supplementation of vitamin D at or above the DRI is an important standard of care in LTC communities [17,26,40,41].

Results from this study determined that several health-related risk factors associated with vitamin D deficiencies are also associated with insufficient levels (< 30 ng/ml). When supplementation rates were compared across various health-related conditions there was no statistically significant difference in the mean daily supplementation rate. However, when mean 25 (OH)D serum levels and health-related conditions were compared, six had significantly different serum levels. Diagnosis of dementia, depression, Alzheimer's, autoimmune disorders, and use of anti-depressants including sertraline (i.e. Zoloft) all had significant difference in mean serum levels when compared to those without a diagnosis. Numerous observational studied have shown these five non-skeletal health-conditions to be associated with vitamin D deficiencies (< 20 ng/ml), but it has yet to be determined if they are a cause-effect relationship [9,42-44]. To the best of our knowledge this study is the first to identify the anti-depressant, sertraline (i.e. Zoloft), as a health-related condition associated with low vitamin D levels. Across the various models (t-test, ANOVA and multiple logistic regression), sertraline, consistently resulted in a significant association with lower serum 25 (OH)D levels. Sertraline was significantly associated with lower mean 25 (OH)D serum levels by 12.2 points and had 3.26 greater odds of having insufficient levels than those not taking the mediation. This association can possibly be explained by examining the metabolic pathway of both 25 (OH)D and sertraline. In the liver, the hydroxylation required to convert bioinert forms of vitamin D into the main circulating form of 25 (OH)D is done via P450 cytochrome enzyme CYP3A4 (25-hydroxylase) [45-47]. CYP3A4 enzyme is the most prevalent enzyme in the liver and it is responsible for metabolizing half of all medications, including

sertraline. CYP3A4 enzyme activity is inhibited by sertraline which results in increased serum concentrations of the medication. Inhibiting CYP3A4 activity results in a decreased hydroxylation of 25 (OH)D, thus decreased serum levels [45-47].

Through logistic regression this study found that Medicaid participants, those taking sertraline, having a diagnosis of Alzheimer's and depression and supplementation below the DRI were all predictors of insufficient 25 (OH)D serum levels. Of these predictors, supplementation below the DRI (800 IU per day) had the strongest association with low serum levels.

Limitations in the study need to be considered when interpreting the results. First, the cross-sectional study design limits inferences on causality of associations. Also, four out of the five communities that participated in the study had the same medical director. So, it reasonable to expect the medical practices and policies of the director would similar across the four communities. Along with the same medical director, four out of the five communities were non-profit (501c3) communities. The Center for Medicare Advocacy states that a community's for-profit or non-profit status should be the key factor in deciding on which LTC community to live in [48]. Extensive research has determined the type of ownership status affects the quality of care the community provides. Research has shown that non-profit LTC communities tend to allocate more resources to resident care, resulting in a better quality of care [48].

Another limitation of the study was the consistency and quality of medical record documentation between communities. For various reasons inadequate and inconsistent medical documentation is common in LTC communities [49,50]. Another limitation of the study included having a limited number of minority participants and fewer Medicaid participants than the general population.

Conclusion

The prevalence of vitamin D insufficiency among LTC residents remained high (56%), despite 60% of the population receiving a daily form of vitamin D supplementation. Several health-related risk factors associated with vitamin D deficient levels (< 20 ng/ml), were also found to be associated with insufficient serum levels (> 30 ng/ml). The results from this study adds to the growing body of evidence that insufficient vitamin D levels are associated with similar non-skeletal conditions of deficient levels such as autoimmune diseases, depression, dementia and Alzheimer's disease [9,12,21,27]. When caring for individuals living in LTC it is important for practitioner to understand that research consistently shows an association between non-skeletal health-related conditions and 2 (OH)D serum levels between < 20 ng/ml and > 30 ng/ml. With vitamin D deficiency affecting 50 - 75% of older adults living in LTC along with the unknown etiology of depression, Alzheimer's, dementia, and autoimmune conditions this study emphasizes the importance of correcting and/or maintaining 25 (OH)D serum levels above > 30 ng/ml [8,9,18,39].

Acknowledgments

The authors would like to thank Brian Haward with Significant Difference LLC for his statistical support and guidance.

Ethical Standards

The study protocol was approved by the Institutional Review Board, University of Texas at Austin (2018-03-0030).

Conflict of Interest

All authors declare no conflict of interest.

Disclaimer

The information presented in the manuscript are mine and not an official position The University of Texas at Austin.

Authorship Agreement

All authors confirm that the manuscript is original work and is unpublished and not under review by any other journal.

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