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ORIGINAL ARTICLE

Gender differences in the prevalence of vitamin D deficiency in a southern Latin American country: a pilot study

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ABSTRACT

Aim: This study aimed to study the prevalence of vitamin D deficiency, assessing the influence of sex, age, and season of the year.

Methods: A cross-sectional study was conducted with 1329 healthy subjects (668 women and 661 men) aged 18–89 years in Santiago, Chile. Age (years), body mass index, medical history, working status, sex, and date of blood sample were collected.

Results: Men were slightly older than women (53.1 ± 18.2 vs. 50.0 ± 15.6 years; $p < 0.01$) and a higher percentage worked outside the home (73.1% vs. 51.9%, $p < 0.001$). The mean serum concentration of 25-hydroxyvitamin D (25(OH)-D) was 23.3 ± 9.3 ng/ml in women and 20.9 ± 9.5 ng/ml in men ($p < 0.001$). The levels of 25(OH)-D by season were 26.7 ± 9.0, 23.6 ± 9.7, 19.4 ± 8.5, and 19.1 ± 9.5 ng/ml (for summer, fall, winter, and spring, respectively; $p < 0.05$). The prevalence of vitamin D deficiency increases with age, rising from 36.5% under 40 years to 48.0% over 60 years ($p < 0.004$). Male sex, winter and spring, and age showed negative correlation with levels of 25(OH)-D ($p < 0.05$). Multivariate linear regression showed a final model that incorporates: age (coefficient: −0.06; 95% confidence interval [CI]: −0.09 to −0.03; $p < 0.001$), male sex (coefficient: −2.00; 95% CI: −2.96 to −1.05; $p < 0.001$), summer (coefficient: 7.30; 95% CI: 6.17 to 8.43; $p < 0.001$), and fall (coefficient: 4.27; 95% CI: 3.04 to 5.50; $p < 0.001$).

Conclusions: Vitamin D deficiency is more prevalent in men than in women, in the elderly, and during the winter and spring seasons.

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Introduction

Between 1922 and 2019 there were 32,285 articles published in PubMed that mentioned the word vitamin D in the title. It is remarkable that 13,033 of these articles have been published in the last 5 years, revealing the increasing importance of this topic[1]. Vitamin D is important in bone and muscle health but has other functions, including cell growth modulation, neuromuscular and immune function, and reduction of inflammation. Thus, low vitamin D levels have been related to an increased risk of various diseases and conditions such as cancer, cardiovascular disease, autoimmune diseases, and diabetes; and even with acute diseases such as infections[2].

As a consequence of population aging, the prevalence of age-related diseases is expected to increase significantly if measures are not taken to mitigate the risks of these diseases[3]. Therefore, knowing the levels of vitamin D in the population, especially in the elderly, and implementing corrective measures is of great relevance to public health as these may affect the risks of musculoskeletal diseases and possibly also other chronic diseases.

As vitamin D has historically been linked to bone health and osteoporotic fractures are more common in women, most epidemiological studies on vitamin D have been conducted in postmenopausal women. A systematic review of vitamin D levels in populations worldwide shows that, of 195 studies conducted in 44 countries with more than 168,000 participants, only 10 studies with 3143 men were conducted specifically in the male population[4]. The same publication points out that only three of the 195 studies, with a total of just over 300 subjects, provided data from Latin America.

Given that we recently published the levels and prevalence of vitamin D deficiency in healthy middle-aged women in Santiago, Chile[5], we were interested in comparing men with women. For this reason, we designed the present study with the aim to assess the prevalence of vitamin D deficiency in a single sample.

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Subjects and methods

Study design

This was a cross-sectional study assessing vitamin D levels in healthy individuals between January 2016 and December 2017. To estimate the sample size, as there is a lack of data on the prevalence of vitamin D deficit in Chilean men, we use the corresponding figures for women (38%)[5]; therefore, with a confidence level of 95%, a minimum of 360 subjects of each sex is required.

Participants and research site

This study was conducted on healthy subjects, aged 18–89 years, randomly selected from those who attended a preventive health control in Santiago, Chile. Subjects complaining with any condition affecting vitamin D levels such as polycystic ovary syndrome, limited daily life activity, disability, or being on a dietary restriction program as well as those with incomplete records were excluded.

The city of Santiago is 520 m above sea level and is located at 33° 24′ S latitude and 70° 40′ W longitude. It has a cool semi-arid climate, with Mediterranean patterns: hot and dry summers with temperatures reaching 35 °C. Winters are cold and humid, with minimum temperatures of around 0 °C and maximum temperatures of 14 °C. Normal annual rainfall is 312 mm.

After obtaining written informed consent and an of-the-moment blood sample for determination of levels of total serum 25-hydroxyvitamin D (25(OH)-D) for each subject, the following data were registered: age (years), body mass index, work, sex, and date. Blood samples according to date were classified according to season of the year (summer, fall, winter, and spring). All of the subjects pertained to medium–high socioeconomic status and were recruited in the private health sector. Venous blood samples were collected between 8:00 and 10:00 am in a standard fasting condition.

Biochemical analysis

Total serum 25(OH)-D was measured using a commercially available electrochemiluminescence immunoassay with a Roche Elecsys 2010 and Cobas E411 platform (Roche Diagnostics GmbH) following the manufacturer's protocol. Duplicate measurements were made for all samples. Range levels of measurements were 3.0–70.0 ng/ml or 7.5–175 nmol/l (1 ng/ml equals 2.5 nmol/l). The functional sensitivity, intra-assay, and inter-assay coefficients of variation for 25(OH)-D are described in detail elsewhere[5]. Circulating 25(OH)-D concentrations were divided into three subgroups according to the 2011 Endocrine Society guideline: deficient (<20 ng/ml), insufficient (20–29 ng/ml), and sufficient (≥30 ng/ml)[6].

Statistical analysis

The data were analyzed using a personal computer-based program (Stata/SE 16.0 for Windows; Stata Corp LLC). For the descriptive analysis, the usual statistics, frequencies, and percentages for qualitative variables and the mean and standard deviation for quantitative variables were used[7]. The Kolmogorov–Smirnov test was used to check the normal distribution of these variables[8].

The age, levels of 25(OH)-D, and season of the year were compared for sex. Pearson's chi-squared test was used to compare frequencies. Student's *t*-test and analysis of variance with Bonferroni correction were used to compare means. Binned scatterplots were used to establish the relationship between levels of 25(OH)-D and age by sex and season of the year[9,10]. The Pearson correlation coefficient was determined between pairs that includes levels of 25(OH)-D, age, and the following dummies variables: male sex, summer, fall, winter, and spring.

From the predictor age and the dummy variables (sex and season of the year), a multivariate linear regression using the ordinary least squares method[10] was done using levels of 25(OH)-D as the dependent variable. The stepwise backward selection approach was used for the selection of predictors in the multivariate linear regression final model[11]. Additionally, for each predictor considered in the final model, their respective linear coefficients and standardized linear coefficients were established. Homoscedasticity was assessed using a plot of residuals versus fitted (predicted) values and by the Breusch–Pagan test[12,13]. Finally, the link test[14,15] and the Ramsey reset test[16] were used to assess the specification error. In addition, as our data can be considered a time series, we performed the Durbin–Watson test and Durbin's alternative test[17,18]. $p < 0.05$ was considered statistically significant.

Ethics

The study was approved by the Ethics Committee of the Faculty of Medicine of the University of Chile. Written informed consent was obtained from all study participants prior to taking a blood sample. This clinical research complied with the principles of the Declaration of Helsinki with respect to human experimentation.

Results

A total of 1491 subjects were recruited; of these, 162 (10.9%) were excluded due to incomplete or wrong records. Thus, the final sample was 1329 subjects, 668 females and 661 males. The levels of 25(OH)-D and age were symmetrically distributed with mean values of 22.1 ± 9.5 ng/ml (men, 20.9 ± 9.5 ng/ml; women, 23.3 ± 9.3 ng/ml; $p < 0.001$) for 25(OH)-D levels and 51.6 ± 17.0 years (women, 50.0 ± 15.6 years; men, 53.1 ± 18.2 years; $p < 0.001$) for age.

The subjects' distribution throughout the seasons for the collection of blood samples was as follows: summer, 351 subjects (26.4%); fall, 279 subjects (21.0%); winter, 322 subjects (24.2%); and spring, 377 subjects (28.4%). The univariate analysis showed that the men were older than the women ($p < 0.01$) and a higher percentage of men worked outside the home (73.1% vs. 51.9%, $p < 0.001$) (Table 1). No

Table 1. Summary of basal characteristics for the 1329 subjects who attended a preventive health control in the city of Santiago, Chile during the period between January 2016 and December 2017.

Characteristic	Women (n = 668)		Men (n = 661)		p-Value (two-tailed)
Age*					
Mean ± SD	50.0 ± 15.6		53.1 ± 18.2		<0.001[b]
Body mass index	27.5 ± 4.7		26.9 ± 5.4		<0.09[d]
Obesity, *n* (%)	205 (30.7)		189 (28.6)		<0.403[c]
Workers, *n* (%)	347 (51.9)		483 (73.1)		<0.001[c]
Levels of 25(OH)-D					
Mean ± SD	23.3 ± 9.3		20.9 ± 9.5		<0.001[a]
Season of year	*n (%)*	*25(OH)-D (ng/ml)*	*n (%)*	*25(OH)-D (ng/ml)*	*p-Value (25(OH)-D)*
Summer	181 (27.1)	26.7 ± 8.8	170 (25.7)	26.6 ± 9.2	<0.955[a]
Fall	143 (21.4)	25.5 ± 9.3	136 (20.6)	21.5 ± 9.6	<0.001[a]
Winter	154 (23.1)	21.0 ± 8.2	168 (25.4)	18.0 ± 8.5	<0.001[a]
Spring	190 (28.4)	20.2 ± 9.1	187(28.3)	18.0 ± 8.2	<0.053[b]

Data are expressed as mean ± standard deviation (SD) and as total numbers and percentage. 25(OH)-D, 25-hydroxyvitamin D.
*Years.
[a]Student's *t*-test assuming equal variance (variance ratio test, $p > 0.05$).
[b]Student's *t*-test assuming unequal variance (variance ratio test, $p < 0.05$).
[c]Pearson's chi-squared test.
[d]Mann–Whitney *U*-test.

differences were observed between males and females regarding body mass index, percentage of obese subjects, or the season they accessed preventive health control.

The mean levels of 25(OH)-D by season were 26.7 ± 9.0, 23.6 ± 9.7, 19.4 ± 8.5, and 19.1 ± 9.5 ng/ml for summer, fall, winter, and spring, respectively. Significant differences were observed between summer and the other seasons and between fall versus winter and spring (Table 1). The prevalence of vitamin D deficiency increases with age, rising from 36.5% under 40 years to 48.0% over 60 years ($p < 0.004$).

Binned scatterplots between 25(OH)-D levels and age suggest a linear relationship between these variables, staying at different levels by sex and season of the year (Figure 1). Note that in the summer more than 95% of men showed levels of 25(OH)-D greater than 20 ng/ml. Age, male sex, winter, and spring showed a negative correlation with levels of 25(OH)-D ($p < 0.05$) whilst summer and fall showed a positive correlation ($p < 0.05$) (Table 2).

The stepwise backward selection approach for predictors on multivariate linear regression showed a final model that incorporated: age (coefficient: −0.06; 95% confidence interval [CI]: −0.09 to −0.03; $p < 0.001$), male sex (coefficient: −2.00; 95% CI: −2.96 to −1.05; $p < 0.001$), summer (coefficient: 7.30; 95% CI: 6.17 to 8.43; $p < 0.001$), and fall (coefficient: 4.27; 95% CI: 3,04 to 5.50; $p < 0.001$). The standardized linear coefficients for the final model were −0.10, −0.11, 0.34, and 0.18 for age, male sex, summer, and fall, respectively.

The individual forecasts for the levels of 25(OH)-D according to the final regression model including predictors (age, male sex, summer, fall, and winter) are shown in Figure 2.

Discussion

This study shows a high prevalence of vitamin D deficiency among men (45.9%). Our results are somewhat different from those shown in a randomly selected subcohort from a large population survey that included men from six US communities where 26% of subjects had levels below 20 ng/ml[19]. Another study which recorded the vitamin D levels of all male patients in a single primary care practice near Boston found that 34% of men had levels below 20 ng/ml[20]. Similar results were observed in a Brazilian study, in which it was found that among the overall population 27.6% of men presented 25(OH)-D levels below 20 ng/ml[21].

Comparing vitamin D deficiency among different population groups is a challenge since the levels of this vitamin can vary depending on social group, geographic location, lifestyle, and so forth[22]. This is evidenced by the fact that the prevalence of vitamin D deficiency in men can reach 87.8% in Saudi Arabia, depending on older age, obesity, sedentary lifestyle, lack of education, poor exposure to sunlight, smoking, and poor dietary vitamin D supplementation[23]. In contrast, in elderly Afro-Caribbean men the deficiency was present in only 2.8% of subjects[24].

In the present study when we compare the prevalence of vitamin D deficiency among men with that observed in women from the same population, in the same laboratory, and in a similar period, we find that men have lower vitamin D levels than women (20.9 ± 9.5 vs. 23.3 ± 9.3 ng/ml, respectively; $p < 0.005$) and that this difference was greater in young adults. Other studies also show that women are no more likely to be deficient in vitamin D than men. One study comparing vitamin D levels in a multiethnic sample in the USA found that the mean levels of 25(OH)-D in men and women were 25.7 and 26.1 ng/ml, respectively[25]. Likewise, evaluating the vitamin D status in healthy Moroccan men and women aged 50 years and older, El Maataoui *et al.* found that vitamin D levels in men and women were similar (20.7 and 20.1 ng/ml, respectively)[26]. Conversely, a study conducted in the Netherlands found that 36% of men over 40 years of age and 51% of postmenopausal women had 25(OH)-D less than 20 ng/ml[27]. Similarly, in New Zealand, in contrast to postmenopausal women, men have low rates of suboptimal vitamin D status, even in winter[28]. These contradictory results aim to show the multiple variables that can affect different populations in vitamin D levels. We can hypothesize from our

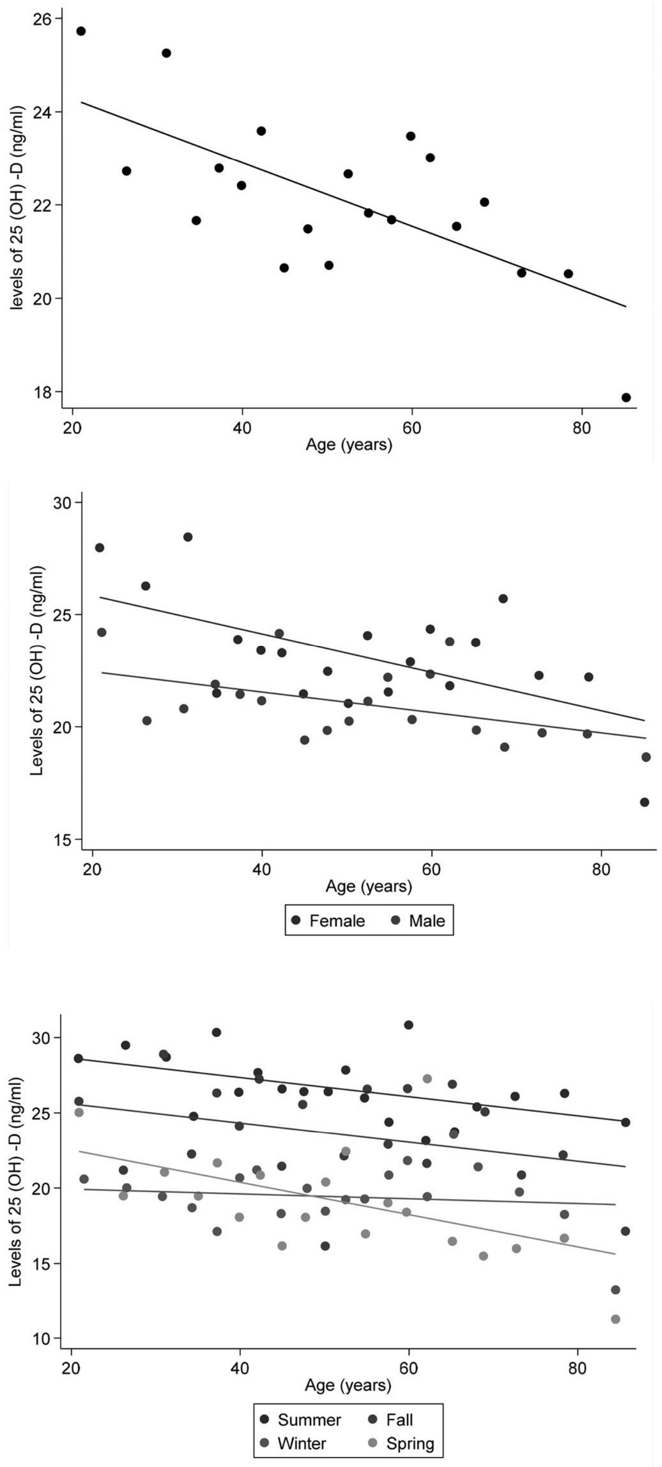

Figure 1. Binned scatterplots showing levels of 25-hydroxyvitamin D (25(OH)-D) and age adjusted by sex and season of the year. Data from 1329 healthy subjects who attended a preventive health control in the city of Santiago, Chile during the period between January 2016 and December 2017.

Table 2. Correlation between levels of 25(OH)-D, age, and the following dummy variables: male sex, summer, fall, winter, and spring.

Variable	*Pearson's correlation coefficient*
Level of 25(OH)-D	
Age	−0.12[a]
Male sex	−0.12[a]
Summer	0.29[a]
Fall	0.08[a]
Winter	−0.16[a]
Spring	−0.20[a]
Age	
Male sex	0.09[a]
Summer	−0.03
Fall	0.02
Winter	0.01
Spring	0.01
Male sex	
Summer	−0.02
Fall	−0.01
Winter	0.03
Spring	−0.01

Data from 1329 subjects who attended to a preventive health control in the city of Santiago (Chile) during the period comprised between January 2016 to December 2017.
[a]$p < 0.05$.

results that the higher prevalence of vitamin D deficiency in men might be due to the fact that among the studied sample there is a higher percentage of male labor force (73.1% men vs. 51.9% women), which implies that men may be less exposed to the sun by spending more time at their workplaces; probably, there are more lifestyle variables that may be influencing our results.

This study showed that the individual forecasts for the levels of 25(OH)-D change according to age, sex, and season of year. Noteworthy, the mean age of men was somewhat higher than that observed in women; however, this difference does not entirely explain the lower level of vitamin D found in men. Multiple linear regression showed that sex was a variable that influences vitamin levels independently of age. Levels of 25(OH)-D were different depending on the season of the year. For example, in summer more than 95% of men show levels of 25(OH)-D greater than 20 ng/ml. In the entire sample, this condition of levels of 25(OH)-D less than 20 ng/ml fluctuates depending on age and sex. In fact, standardized regression coefficients of the sample reinforce these data. The sun exposure time is a relevant factor to be considered when levels of 25(OH)-D are determined. It is noteworthy that in Chile the ultraviolet index fluctuates between December (beginning of summer) and June (beginning of winter) between 6.4 and 1.5, respectively; the UV-B radiation being 16 and 4 $\mu W/cm^2$ in those months[29]. Therefore, the variability of vitamin D levels in different seasons of the year is not surprising.

We also found differences in prevalence of vitamin D deficiency between men and women. Although we do not study the factors that could explain this difference, we could hypothesize different reasons. First, fashion and dress customs in women might be related to greater sun exposure in young women. Second, male sedentarism; The National Health Survey revealed that in Chile 92.5% of men between 30 and 49 years of age are sedentary versus 86.2% of women of the same age group (significant difference with 95% confidence)[30].

A Canadian study, in which vitamin D supplementation was allowed, also found a higher prevalence of vitamin D deficiency in men in both summer and winter (5.7% and 12.6% in men vs. 1.9% and 8.7% in women, respectively)[31]. Conversely, the previously mentioned Dutch study noted that in summer men had significantly higher levels of 25(OH)-D as compared to women (32.6 vs. 21.3 ng/ml)[27].

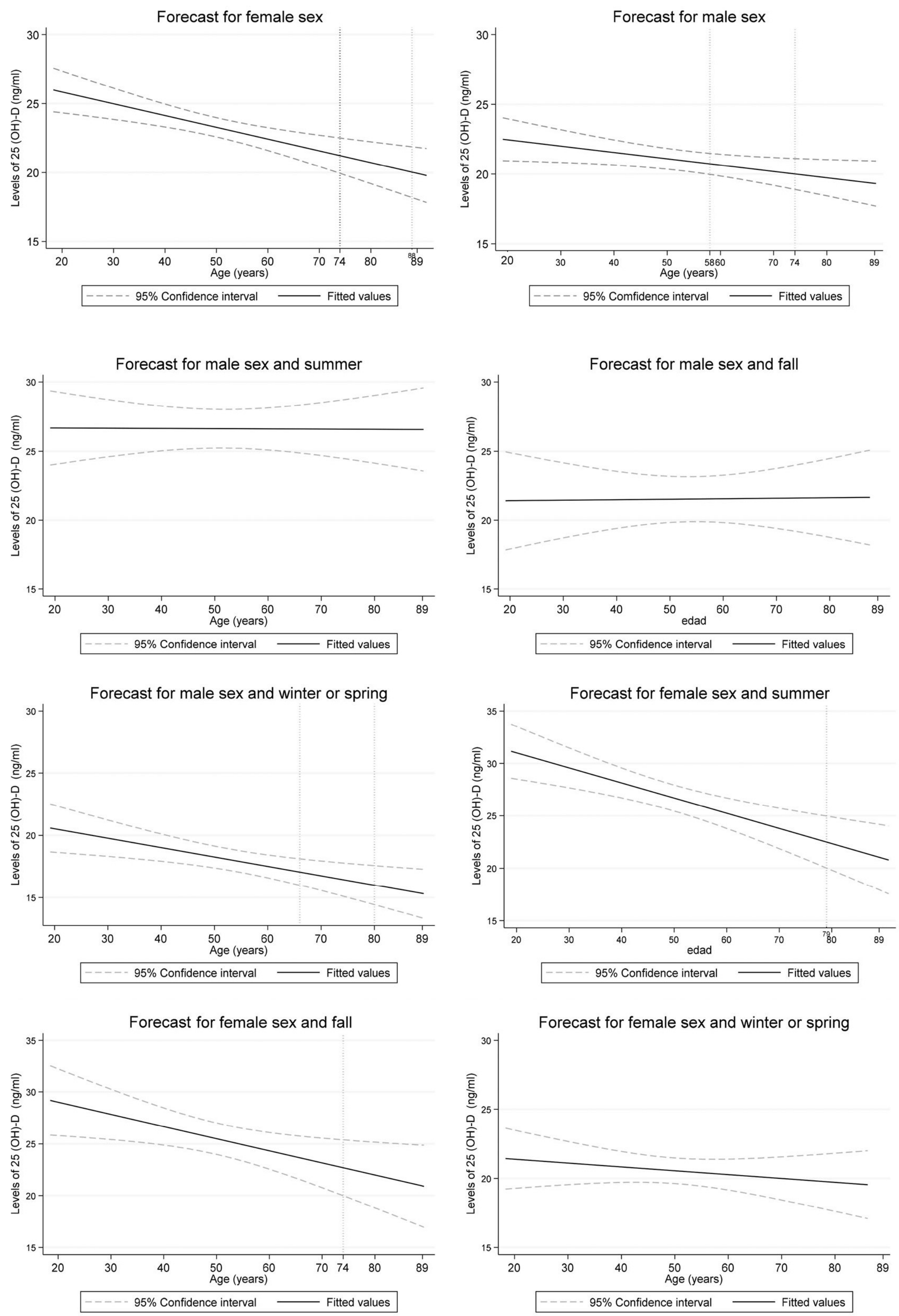

Figure 2. Individual forecast of 25-hydroxyvitamin D (25(OH)-D) levels according to the final regression model including age, male sex, summer, fall, and winter predictors.

Interestingly, vitamin D levels did not recover quickly in spring. This fact is in agreement with previous data. Different studies in England[32] and South Alaska[33] showed the same seasonal pattern. These observations would indicate latency in the recovery of plasma levels of vitamin D.

The variability of results obtained in the different studies indicates the multiplicity of factors that can determine vitamin D levels in different populations. However, this does not invalidate the results obtained in the different studies. Therefore, specific health policies adapted to the local reality should be established in countries. In this study, the results indicate a high prevalence of vitamin D deficiency in the male population and suggest the need to introduce measures to reduce related population risks.

A weakness of this study is that it uses a convenience sample of consultant 'healthy' subjects (annual check-up), which may have various selection biases. Therefore, it does not reflect the vitamin D status of the entire population of Chile. However, since the clinic of the University of Chile is a health center that serves Chile's middle class (47% of the population[34]) it is a median reflection, although not accurate, of the entire population. Another limitation of our study is that we have not measured the change in vitamin D levels over time in the same individuals and we did not record the sun exposure times or diet, factors that may be involved in the observed differences. Our goal was to describe the prevalence and the seasonal variations by age only. It is now warranted to evaluate the influence of the aforementioned factors on the results we have described.

Conclusions

The authors could conclude that in Chile, a southern country, there is a high prevalence of vitamin D deficiency in men of all ages and that this deficit is greater in men than in women, especially during the winter months.

Potential conflict of interest J. E. Blümel received support from Grünenthal for attending the IMS Congress 2018, Vancouver. C. Castelo-Branco received Honoraria from Italfarmaco Spain, FAES, and Theramex. M. S. Vallejo, E. Arteaga, S. Aedo, V. Tapia, A. Araos, and C. Sciaraffia declare that they have no conflict of interest.

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Data reference

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