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# VITAMIN D LEVELS OF OUTPATIENTS ADMITTED TO A UNIVERSITY HOSPITAL IN THE MARMARA REGION OF TURKEY OVER 3 YEARS

## NIVOI VITAMINA D KOD VANBOLNIČKIH PACIJENATA PRIMANIH NA UNIVERZITETSKU KLINIKU U MARMARA REGIONU U TURSKOJ U PERIODU OD 3 GODINE

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### Summary

**Background:** Vitamin D regulates calcium and phosphorus metabolism, and it is essential for bone formation. Several factors can affect vitamin D levels in plasma. In present study we compare vitamin D levels of outpatients, who admit to Maltepe University Hospital between 2011 and 2013 and had vitamin D measurements regarding gender, age, and season.
**Methods:** Hospital records were evaluated to identify the outpatients with vitamin D levels and their gender, age, and vitamin D levels and the seasons of measurements were recorded.
**Results:** Data of 4860 subjects (74% female) were analyzed and 69.2% were between 18–64 years old. Vitamin D levels were as follows: 43.1% ≤ 10 ng/mL, 31.9% between 10 ng/mL and 20 ng/mL, 16.1% between 20 ng/mL and 30 ng/mL, and only 8.9% ≥ 30 ng/mL. The number of females with vitamin D levels < 10 ng/mL was significantly higher than that of males, while the number of males with vitamin D levels between 10 ng/mL and 20 ng/mL was significantly higher than that of females (P = 0.001) for each of the individuals, 6.2% and 11.1% had sufficient levels in winter and summer, respectively. Overall, it was observed that 6.6% of individuals between 18–44 years old, 8.2% of individuals between 45–64 years old and 10.3% of individuals over 65 years old had vitamin D levels > 30 ng/mL.
**Conclusions:** The prevalence of vitamin D deficiency in outpatients of Maltepe University Hospital in Marmara region was 75% (< 20 ng/mL).

**Keywords:** vitamin D, season, gender, age

### Kratak sadržaj

**Uvod:** Vitamin D reguliše metabolizme kalcijuma i fosfora i od esencijelne je važnosti za formiranje kostiju. Više faktora može da utiče na nivoe vitamina D u plazmi. U ovom radu upoređivani su nivoi vitamina D kod vanbolničkih pacijenata, koji su primani u Maltepe Univerzitetsku bolnicu između 2011 i 2013, a kojima je vitamin D meren zavisno od pola, starosti i godišnjeg doba.
**Metode:** U bolničkim kartonima evidentirani su podaci o identitetu vanbolničkih pacijenata kao i njihov pol, godine starosti, nivo vitamina D i godišnje doba u vreme merenja.
**Rezultati:** Podaci 4860 osoba (74% ženskih) od kojih su 69,2% bile starosti između 18–64 godine. Nivoi vitamina D bili su slede I: 43,1% ≤ 10 ng/mL, 31,9% između 10 ng/mL i 20 ng/mL, 16,1% između 20 ng/mL i 30 ng/mL, a samo 8,9% ≥ 30 ng/mL. Broj žena sa nivoima vitamina D < 10 ng/mL bio je značajno viši nego kod muškaraca, dok je broj muškaraca sa nivoima vitamina D između 10 ng/mL i 20 ng/mL bio značajno viši nego kod žerna (P = 0,001) kod svake osobe, 6,2% i 11,1% imali su dovoljne nivoe tokom zimskog perioda, kao i leti. Ukupo gledaju i, uočeno je da 6,6% osoba između 45–64 godina starosti, 8,2% osoba između 45–64 godina starosti i 10,3% osoba iznad 65 godina starosti imao je nivo vitamina D > 30 ng/mL.
**Zaključak:** Učestalost deficijencije vitamina D kod vanbolničkih pacijenata ispitivanih u Maltepe Univerzitetskoj bolnici u regionu Marmare iznosila je 75% (< 20 ng/mL).

**Ključne reči:** vitamin D, godišnje doba, pol, starost

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## Introduction

Vitamin D is an essential nutrient that plays a major role in human health from birth to death. Two major forms of vitamin D important for humans are vitamin D3, so called cholecalciferol and vitamin D2, also known as ergocalciferol (1). The major role of vitamin D in the body is maintaining calcium, iron, magnesium, phosphate and zinc levels by regulating intestinal absorption (1, 2), and its deficiency results in rickets, osteomalacia and osteoporosis and it is thought that the risk of developing cardiovascular, auto-immune and endocrine diseases and cancer increase in case of deficiency (3, 4). The most accurate method of evaluating a person's vitamin D status is to measure the level of serum 25-hydroxyvitamin D (25(OH)D). According to the US Endocrine Society Clinical Practice guideline published in 2011 (1, 5), vitamin D deficiency is defined as 25(OH)D less than 20 ng/mL (50 nmol/L), vitamin D insufficiency is defined as levels between 21 ng/mL and 29 ng/mL. A blood level of 25(OH)D should be greater than 30 ng/mL to minimize the risk of hypercalcemia as 100 ng/mL (250 nmol/L).

Vitamin D is different from other essential vitamins, because besides dietary intake, the body can manufacture it with sunlight exposure. Sources of vitamin D-rich food mainly include oily fish and dairy products. There are also vitamin D fortified food products in some countries like USA, however it has been reported that consumption of these food products are not enough to meet the daily recommended levels (6). Given the fear of developing skin cancer, many individuals avoid exposure to sunlight; hence, vitamin D deficiency has become a global concern, considering its role in human health, and it has been reported that the prevalence of vitamin D deficiency ranges from 2 to 90% depending on the cut-off value and study population selected (4).

Multiple factors have been associated with lower vitamin D levels, including gender, age, obesity, skin type, pigmentation, ethnicity, smoking, sedentary life, the season the measurement was made and the geographic region (7–10).

In the present retrospective study, vitamin D levels of patients who were admitted to Maltepe University Hospital between 2011 and 2013 and had vitamin D measurements, were evaluated according to gender, age and the season in which the measurement was made and the department that made the request.

## Materials and Methods

*Patients*

In this retrospective hospital-based study, the hospital registries of Maltepe University Hospital between 2011 and 2013 were evaluated, after approval was obtained from the Ethics Committee of Kartal Training and Research Hospital (Decision No: 4, 12.03.2013). The outpatients, who were admitted to the different departments of the hospital and were requested vitamin D levels, were identified, and their gender, age, vitamin D levels, the department that made the request and the season in which (winter and summer) the measurement was made were recorded.

*Statistical Analysis*

Statistical analysis was performed using NCSS (Number Cruncher Statistical System) 2007 & PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA). While analyzing data, in the comparison of quantitative data as well as descriptive statistical methods (mean, standard deviation, median, frequency rate) between two comparison groups, Mann-Whitney U test is used; the Kruskal-Wallis test is used in the comparison of three or more groups; and Mann-Whitney U test was used for determining the group which causes the difference. In the comparison of qualitative data Pearson's chi-square test was used. A P value $<0.05$ was considered to be statistically significant.

## Results

In the present study, the data of 4860 subjects, 74% female, were analyzed. Most of the subjects were between 18 and 64 years of age (69.2%), only 5.7% being below 18 years of age. Vitamin D measurements were performed in winter in 44.9% (n = 2183) of the subjects and in summer in 55.1% (n = 2677) of them.

Vitamin D measurements were performed on request of Internal Disease Department in 46.6%, (n = 2263), Physical Therapy and Rehabilitation Department in 15.3% (n = 743), Endocrine Department in 12.2% (n = 593) and Psychiatry Department in 9.5% (n = 462). The remaining 16.4% of the measurements were done on requests of different departments of the hospital. Vitamin D levels of patients with chronic renal failure and hepatic failure were not included in the study.

Vitamin D levels of the subjects were as follows, 43.1% (n = 2093) at or below 10 ng/mL, 31.9% (n = 1551) between 10 ng/mL and 20 ng/mL, 16.1% (n = 783) between 20 ng/mL and 30 ng/mL and only 8.9% (n = 433) at or above 30 ng/mL. The demographic characteristics of the study population are presented in *Table I*.

The vitamin D measurements of the women subjects vary between 3 to 100 with an average of $14.10 \pm 11.55$ and median of 10.92. The vitamin D measurements of the men subjects vary between 3 to

100 with an average of 16.26 ± 10.94 and median of 14.47. Therefore, it was found that according to gender the difference between vitamin D measurements was statistically significant ($p < 0.01$). When compared to those of women, the vitamin D measurements of men subjects are significantly higher. This significant difference resulted from ones whose vitamin D levels were 10 or below, and that the proportion of vitamin level 10 or below of women was more significant than those of men ($p < 0.01$). Furthermore, the percentages of the men subject's vitamin D levels at or above 30 ng/mL were higher than women's. However, this result showed no significant difference according to gender ($p > 0.05$). The distribution of study subjects according to gender and vitamin D levels is presented in *Table II*.

The vitamin D measurements of the subjects who were admitted in the winter vary between 3 to 100 with an average of 13.27 ± 10.45 and median of 10.56. The vitamin D measurements of the subjects who were admitted in the summer vary between 3 to 100 with an average of 15.79 ± 12.06 and median of 13.30 (*Table III*). Therefore, it was found that according to seasons the difference between vitamin D measurements was statistically significant ($p < 0.01$). When compared to those of subjects admitted in winter, the vitamin D measurements of subjects admitted in the summer are significantly higher and the difference was found to be significant according to the seasons ($p = 0.001$). The percentage of those with Vitamin D levels lower than 10 ng/mL was higher in winter than in summer. While there was no difference between the percentages of subjects with values between 10–20 ng/mL, the vitamin D levels of those who were 20–30 ng/mL and above 30 ng/mL were higher in summer than in winter ($p < 0.01$). The distribution of subjects according to vitamin D levels and the season of estimation is presented in *Table III*.

It was found that there was significant difference among the vitamin D measurements of female subjects according to age groups ($p < 0.01$). According to the dual comparison conducted to identify the group that caused the difference, the vitamin D measurements of subjects 1 year or below years of age are significantly higher than those of 6.1–17.0 years of age, 18–44 years of age, 45–64 years of age, and 65 and above ($p < 0.01$), whereas the vitamin D measurements of subjects 1.1–6.0 years of age are significantly higher than those of 6.1–17.0 years of age, 18–44 years of age, 45–64 years of age, and 65 and above ($p < 0.01$). The vitamin D measurements of subjects in the age group of 65 and above was significantly less than those of 18–44 years of age, 45–64 years of age ($p < 0.01$). The dis-

**Table I** Demographic characteristics of the study population.

| | | n | % |
|---|---|---|---|
| Gender | Female | 3597 | 74 |
| | Male | 1263 | 26 |
| Department | Internal disease | 2263 | 46.6 |
| | Psychiatry | 462 | 9.5 |
| | Physical Therapy and Rehabilitation | 743 | 15.3 |
| | Endocrine | 593 | 12.2 |
| | Nephrology | 203 | 4.2 |
| | Chest Diseases | 241 | 5.0 |
| | Pediatrics | 203 | 4.2 |
| | Medical Oncology | 152 | 3.1 |
| Vitamin D level (ng/mL) | ≤ 10 | 2093 | 43.1 |
| | 10 – 20 | 1551 | 31.9 |
| | 20 – 30 | 783 | 16.1 |
| | 30 | 433 | 8.9 |

**Table II** Distribution of the subjects according to gender and vitamin D levels.

| | | Gender | | P | Post Hoc Test |
|---|---|---|---|---|---|
| | | Female (n = 3597) | Male (n = 1263) | | |
| Vitamin D level (ng/mL) | Min-Max<br>Mean ± SD<br>Median | 3.0–100.0<br>14.10±11.55<br>10.92 | 3.0–100.0<br>16.26±10.94<br>14.47 | $^{a}$0.001** | |
| Vitamin D level (ng/mL) n (%) | < 10 | 1682 (46.8) | 411 (32.5) | $^{b}$0.001** | $^{1 \text{ vs } (2+3+4)}$p<0.01** |
| | 10 – 20 | 1059 (29.4) | 492 (39.0) | | $^{2 \text{ vs } (1+3+4)}$p<0.01** |
| | 20 – 30 | 552 (15.3) | 231 (18.3) | | $^{3 \text{ vs } (1+2+4)}$p<0.05 |
| | > 30 | 304 (8.5) | 129 (10.2) | | $^{4 \text{ vs } (1+2+3)}$p>0.05 |

$^{a}$Mann Whitney U Test, vs: versus, $^{b}$Pearson Chi-Square Test, **p<0.01

**Table III** Distribution of subjects according to vitamin D levels and season.

| | | Seasons | | P | Post Hoc Test |
|---|---|---|---|---|---|
| | | Winter (n = 2183) | Summer (n = 2677) | | |
| Vitamin D level (ng/mL) | Min-Max<br>Mean ± SD<br>Median | 3.0–100.0<br>13.27±10.45<br>10.56 | 3.0–98.9<br>15.79±12.06<br>13.30 | [a]0.001** | |
| Vitamin D level (ng/mL) n (%) | < 10 | 1040 (47.6) | 1053 (39.3) | [b]0.001** | 1 vs (2+3+4) p<0.01** |
| | 10 – 20 | 710 (32.5) | 841 (31.4) | | 2 vs (1+3+4) p>0.05 |
| | 20 – 30 | 297 (13.6) | 486 (18.2) | | 3 vs (1+2+4) p<0.01** |
| | > 30 | 136 (6.2) | 297 (11.1) | | 4 vs (1+2+3) p<0.01** |

[a]Mann Whitney U Test, vs: versus, [b]Pearson Chi-Square Test, **p<0.01

**Table IV** Distribution of the subjects according to vitamin D levels and age groups.

| Vitamin D level (ng/mL) | Age groups (years) | | | | | | |
|---|---|---|---|---|---|---|---|
| | ≤1 (n = 27) | 1.1 – 6 (n = 52) | 6.1 – 17 (n = 195) | 18 – 44 (n = 1771) | 45 – 64 (n = 1596) | 65 (n = 1219) | P |
| Min–Max | 4.0–100 | 4.0–60.9 | 3.0–52.6 | 3.0–75.7 | 3.0–70.0 | 3.0–100.0 | [a]0.001** |
| Mean | 34.22 | 29.57 | 18.43 | 13.82 | 14.67 | 14.20 | |
| SD | 19.46 | 13.80 | 10.66 | 10.11 | 10.71 | 12.91 | |
| Median | 29.06 | 26.21 | 16.95 | 11.40 | 12.51 | 10.10 | |
| < 10; n (%) | 1 (3.7) | 3 (5.8) | 49 (25.1) | 784 (44.3) | 651 (40.8) | 605 (49.6) | [b]0.001** |
| 10 – 20; n (%) | 4 (14.8) | 8 (15.4) | 68 (34.9) | 602 (34.0) | 539 (33.8) | 330 (27.1) | |
| 20 – 30; n (%) | 10 (37.0) | 21 (40.4) | 51 (26.2) | 268 (15.1) | 275 (17.2) | 158 (13.0) | |
| > 30; n (%) | 12 (44.4) | 20 (38.5) | 27 (13.8) | 117 (6.6) | 131 (8.2) | 126 (10.3) | |

[a]Kruskal Wallis Test, [b]Pearson Chi-Square Test, **p<0.01

tribution of study subjects according to vitamin D levels and age groups is shown in *Table IV*.

It was observed that vitamin D levels decreased with age. Considering the vitamin D levels which are most distributed number of subjects according to age groups; vitamin D levels were found less than 10 ng/mL in 49.6% of the subjects aged 65 years and over, 40.8% of the subjects aged 45–64 and 44.3% of the subjects aged 18–44 years (p < 0.01). Vitamin D levels were found 10–20 ng/mL in 34.9% of the subjects in the age range of 6.1–17 years and 40.4% of the subjects in the age range of 1.1–6 years were found 20–30 ng/mL. Vitamin D levels were observed more than 30 ng/mL in 44.4% of the subjects 1 and below year of age (*Table IV*). While in the age group under 1 year and 1.1–6 years old no statistically significant difference was found between vitamin D levels according to seasons (p > 0.05), in the age groups 6–17, 18–44 and 45–64 vitamin D levels was found significantly high in summer (p < 0.01). Non statistically significant difference was found in 65 or above years of age according to the seasons (p > 0.05). In both male and female subjects, it was found that vitamin D levels in summer were significantly high (p < 0.01). The distribution of age and gender according to seasons is shown in *Table V*.

**Table V** Distribution of age and gender according to seasons.

| | Vitamin D level (ng/mL) | | p |
|---|---|---|---|
| | Winter (n=2183)<br>Mean ±SD (median) | Summer (n=2677)<br>Mean ± SD (median) | |
| ≤1 age | 34.70±25.23 (26.8) | 33.82±14.23 (29.7) | 0.558 |
| 1.1 – 6 age | 26.66±13.15 (24.7) | 32.48±14.07 (27.2) | 0.173 |
| 6.1 – 17 age | 15.26±8.39 (13.9) | 20.97±11.61 (19.8) | 0.001** |
| 18 – 44 age | 11.86±8.81 (9.4) | 15.21±10.73 (13.6) | 0.001** |
| 45 – 64 age | 13.33±9.56 (11.4) | 15.87±11.53 (13.6) | 0.001** |
| ≥65 age | 13.65±12.08 (10.1) | 14.67±13.69 (10.1) | 0.565 |
| Female | 12.80±10.22 (9.9) | 15.15±10.43 (12.0) | 0.001** |
| Male | 14.59±10.96 (12.5) | 17.65±10.73 (16.1) | 0.001 |

**Mann Whitney U test, **p<0.01

## Discussion

In this retrospective study, the registries of patients who were admitted to the different departments of Maltepe University hospital between 2011 and 2013 and had vitamin D measurements were analyzed, and the prevalence of vitamin D deficiency was found as 76.2% in females and 71.5% in males, and vitamin D insufficiency as 15.3% in females and 18.3% in males.

More than one-third of the studies related to vitamin D status have been reported mean values below 50 nmol/L (4), and the prevalence varies considerably across countries. A recent review by Lips evaluating vitamin D status in Europe and Asia, reported a north south gradient in vitamin D levels, the levels being high in Scandinavian countries and low in Italy, Spain and some other Mediterranean countries (11). However, there are also variations among countries in the same geographic region; while vitamin D is deficient in 77% of Estonians in winter, the overall prevalence is 40% in Norway, and 34% in Sweden, all being North European countries (8, 12, 13). The lower rates that were observed in Norway and Sweden were attributed to the consumption of fatty fish. A study of Burgaz et al. (14) in Swedish women reported that, of the dietary factors, the main food groups that showed the best correlation with 25(OH)D serum concentrations were fatty fish and vitamin D-fortified reduced-fat dairy products.

The prevalence was found to be 22.7% in South Australia (15), 24% in Brazil (16), while the prevalence of vitamin D deficiency in adolescents was found to be 45.4 % in the United Arab Emirates (17). Nevertheless, the prevalence of vitamin D deficiency was 78.1% in females and 72.4% in males in Saudi Arabia, located in the Middle East as is the United Arab Emirates (18). It has been reported that 70% to 90% of the individuals living in India, Iran, and in some countries in South Asia had vitamin D deficiency (7, 19, 20). The higher prevalence observed in these countries, was associated with lifestyle patterns developed according to social, cultural and religious beliefs like clothing and vegetarianism. A study performed by Alagol et al. (21) on Turkish women, investigated the efficiency of sunlight exposure in 48 premenopausal women, in relation to 3 different types of dressing in summer. Women in the first group were dressed in a style which exposed the usual areas of the skin to sunlight; those in the second group wore traditional clothing with the skin of the hands and face uncovered, while the third group of women was dressed in traditional Islamic style, covering the whole body including hands and face. It was found that while, 44% of those in Group I and 60% of those in Group II, had vitamin D deficiency, all women in group III had vitamin D levels below normal (21).

Numerous studies reported higher vitamin D levels in men than women (22, 23). This finding might have a few possible reasons: women tend to have more body fat than men, they spend a bit more time indoors, and they tend to have sun protection behavior because of cosmetic concerns. Additionally, in Muslim countries, women wear veils and special clothing covering the whole body according to religious beliefs, therefore they have no exposure to sunlight, which is one of the sources of vitamin D (24). However, in a study in North Iran, the prevalence of vitamin D deficiency was similar in males and females (7), and a study comparing serum 25(OH)D levels from the Third National Health and Nutrition Examination Survey (NHANES) collected between 1988 and 2004 with the levels from NHANES 2001–2004, reported that while males had higher vitamin D levels than females in 1988–1994 cohort, sex-related difference was equalized in 2001–2004. The authors stated that this might be secondary to disproportionately greater time indoors and less time outdoors among males compared with females (25). Similar to the majority of the studies, the rate of vitamin D deficiency was significantly higher in females in comparison to males in the present study.

As was mentioned above, sunlight is one of the main sources of vitamin D. The level of cutaneous vitamin D3 synthesis in the skin is associated with the amount of solar UVB radiation, which is affected by the geographic latitude, season of the year and time of day (2). Additionally, cutaneous synthesis decreases with increasing age, due to a decrease in 7-dehydrocholesterol levels and morphological changes due to biological aging. It was reported that while 20% of the individuals had deficient vitamin D levels in summer, the rate increased to 64% in Norway (8), a Scandinavian country, and while 22% of individuals had vitamin D deficiency in summer, the corresponding rate was 38% in males and 40% in females in South Florida, so called the Sunshine State (26). However, a study performed in North Iran, reported that there was no significant difference in vitamin D levels measured in different seasons (5). While 80.1% of the outpatients that had vitamin D measurements during winter had vitamin D deficiency, the rate decreased to 70.7% in summer in the present study. The relatively small difference across seasons found in the present study might be due to clothing worn by the women according to religious beliefs.

Serum vitamin D levels are also associated with age, and as people get older, cutaneous synthesis and absorption of vitamin D decreases. Also, advanced age leads to reduced activity, which gives elderly less opportunity to be outdoors. Studies report conflicting results about the relation between age and vitamin D levels. The study comparing NHANES 1988–2004 data with NHANES 2001–2004 data reported that besides gender-related differences, age-related differences also disappeared in 2001–2004 cohort, probably due to spending more time indoors (25). A study performed by Meyer et al. (27) reported that age was not related with vitamin D levels in Sri Lankans and native of Norway while Laktasic-Zerjavic et al. (9) in their study in Croatia and Alfawaz et al. (18) in their study in Saudi Arabia reported that the rate of vitamin D deficiency increase with increasing age; however Heidari Behzad et al. (7) in their study performed in North Iran reported that serum vitamin D levels increase with increasing age. In the present study, similar to (28, 29), the rate of vitamin D deficiency increased with increasing age. While 40.5 of subjects below 6 years of age had sufficient vitamin D levels, only 7.4% of subjects between 18 and 64 years of age and 10.3% of subjects over 65 years of age had sufficient vitamin D levels. The relatively higher levels in children below 6 years of age may be due to intake of vitamin D products and consumption of dairy products.

This study although evaluated vitamin D levels of a large sample size of subjects has some limitations as it is a hospital based study with retrospective nature. Limited information can be obtained from hospital registries and the analysis was performed on blood samples of patients who were admitted to the hospital because of different complaints, and vitamin D measurement results concluded that there might be deficiency of this essential vitamin among the subjects under different age groups. However, patients from all parts of Marmara region are admitted to the Maltepe university Hospital located in the north west of Turkey in Marmara region. The prevalence of 75% (<20 ng/mL) found in the present retrospective study was similar to the prevalence found by Hekimsoy et al. (30) in a cross-sectional study performed in the Aegean region of Turkey. Hence, it may be concluded that the prevalence of vitamin D deficiency is around 75% in Turkey, a Mediterranean country. In this study, vitamin D status was affected by gender, season and age. When vitamin D levels were compared according to gender, it was found that the proportion of females with vitamin D levels with 10 ng/mL or below 10 ng/mL was significantly higher than that of males. The proportion of males with vitamin D levels between 10 ng/mL and 20 ng/mL and those with vitamin D levels between 20 ng/mL and 30 ng/mL were significantly higher than that of females. On the other hand, the proportion between males and females with levels above 30 ng/mL were not of significant difference. Moreover, according to seasons, it was observed that while 6.2% of the individuals have sufficient vitamin D levels (>30 ng/mL) in winter, this rate increased to 11.1% in summer. In addition, when vitamin D levels of the subjects were evaluated according to age groups, it was found that 38.5% of subjects between 1.1–6 years of age had sufficient levels (> 30 ng/mL), this rate was only 13.8% among the individuals between 6.1–17 age, 6.6% among the individuals between 18–44 age, 8.2% in 45–64 age and 10.3% among the individuals over 65 years of age.

## Conflict of interest statement

The authors stated that they have no conflicts of interest regarding the publication of this article.

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