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Original article

The burden of vitamin D deficiency in a mediterranean country without a policy of food fortification

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Summary. *Background:* Vitamin D deficiency is a public healthcare issue and its correction is increasingly regarded as a cornerstone of preventive medicine. *Methods:* We designed a retrospective observational study to clearly define the burden of total vitamin D (25-hydroxyvitamin D) deficiency in a supposedly healthy population of outpatients residing in two regions (Emilia Romagna and Veneto) of Northern Italy. *Results:* 25-hydroxyvitamin D results were available for a total number of 5,096 outpatients in the two centers. The median value of 25-hydroxyvitamin D was 60 nmol/L, and was higher in women than in men (62 nmol/L versus 56 nmol/L; p<0.001). The rate of 25-hydroxyvitamin D deficiency was 36%, and was marginally but significantly higher in men than in women (40% versus 35%; p=0.003). A significant variation in the rate of 25-hydroxyvitamin D deficiency was found throughout different age ranges, exhibiting a significant increase in the elderly. *Conclusions:* The results of this large observational study show that the burden of 25-hydroxyvitamin D deficiency in two regions of a Mediterranean country without a policy of food fortification is as high as 36%, and this evidence represents a background for healthcare preventive measures aimed at reducing the prevalence of this condition in the general population. (www.actabiomedica.it)

Key words: vitamin D, deficiency, deficit, prevention

Introduction

Vitamin D is a fat-soluble compound which regulates calcium homeostasis and is also of vital importance for muscle development, function and preservation (1). Recent evidence also indicates that vitamin D status may strongly influence the risk of a number of severe human disorders such as cancer, diabetes and cardiovascular disease (1,2). In humans, the active pool of vitamin D is strongly regulated by diet and dermal synthesis, so that environmental changes may exert a substantial impact on its concentration and bioavailability.

Although epidemiological data about the burden of total vitamin D (25-hydroxyvitamin D) deficiency are considerably heterogeneous around the globe, several lines of evidence seemingly attest that this condition may be more frequent than expected (3). Moreover, its prevalence is continuously increasing due to considerable lifestyle changes that have occurred over the past decades, and which are basically attributable to lower exposure to sun irradiation and changes of dietary habits (3). To overcome the increasing burden of 25-hydroxyvitamin D deficiency, several countries such as the US and Canada have developed specific policies of vitamin D food fortification (4). Nevertheless, the usage of supplements as well as the vitamin D content of available supplements in many of these countries remained low, so that even food fortification

failed to reach the expected target of reducing vitamin D deficiency (5).

One of the mainstay of preventive medicine is to clearly identify the burden of a given phenomenon and then recognize and correct the underlying causes. Therefore, we designed a retrospective observational study to clearly define the frequency of 25-hydroxyvitamin D deficiency in an supposedly healthy population of outpatients residing in two regions (Emilia Romagna and Veneto) of the Northern Italy.

Materials and methods

We performed a retrospective search in the laboratory information systems of two different University Hospitals located in northern Italy (Verona, north-east Italy and Parma, north-west Italy), to identify available data of total serum vitamin D (25-hydroxyvitamin D) in outpatients referred for routine health check-up during the year 2013. In both centers 25-hydroxyvitamin-D was measured with an identical competitive chemiluminescence assay (Liaison, DiaSorin, Saluggia, Italy). The alignment and correspondence of results was validated throughout the study period using the same materials for internal quality control (IQC) and external assessment scheme (EQA). Results were expressed as median and interquartile range (IQR). The 25-hydroxyvitamin D deficiency was defined as a serum concentration of 25-hydroxyvitamin D level <50 nmol/L (i.e., 20 ng/mL), in agreement with the current recommendations of the International Osteoporosis Foundation (IOF) (6). Differences between patients cohorts were evaluated using ANOVA (for continuous variables) and Pearson's χ^2 test with Yates' correction (for categorical variables), using Analyse.it (Analyse-it Software Ltd, Leeds, UK). The study was performed in accordance with the Declaration of Helsinki, under the terms of relevant local legislation.

Results

25-hydroxyvitamin D results were available for a total number of 5,096 outpatients in the two centers (3,042 from Verona and 2,054 from Parma, respectively). The median value of 25-hydroxyvitamin D in the entire study population was 60 nmol/L (38-81 nmol/L), and it was found to be higher in women (n=3,859; 62 nmol/L; IQR, 39-83 nmol/L) than in men (n=1,237; 56 nmol/L; IQR, 38-75 nmol/L; p<0.001). The rate of 25-hydroxyvitamin D deficiency in the entire study population was 36% (1,856/5,096), and it was found to be marginally but significantly higher in men than in women (40% versus 35%; p=0.003). Interestingly, the rate of severe 25-hydroxyvitamin D deficiency (i.e., <25 nmol/L) in the entire study cohort was 13% (639/5,096). The median value of 25-hydroxyvitamin D (59 nmol/L in Parma versus 61 nmol/L in Verona; p=0.256) and the rate of 25-hydroxyvitamin D deficiency (38% in Parma versus 35% in Verona; p=0.162) were found to be similar between the two centers. Although the values of 25-hydroxyvitamin D exhibited a significant variation across different age ranges in the entire study population (p=0.001 for trend) (Fig. 1), the difference remained significant in the female cohort (p<0.001) but not in the male cohort (p=0.215). A significant variation in the rate of 25-hydroxyvitamin D deficiency was also found in the entire study population (1-15 years, 26%; 16-30 years, 33%; 31-45 years, 41%; 46-60 years, 37%; 61-75 years, 36%; 76-90 years, 39%; >90 years, 53%) (p=0.001), and this difference remained statistically significant in both the female (p<0.001) and male (p=0.008) cohorts.

Discussion

Vitamin D status depends on a number of genetic, lifestyle and geographical factors, which include gender, age, skin pigmentation, exposure to sunlight, dietary habits, supplement intake and physical exercise (7). The 25-hydroxyvitamin D deficiency is now recognized as a public health care issues, due to its important association with reduced bone mineral density, frailty, cancer, diabetes and cardiovascular disease (1,2). Therefore, an accurate and timely identification of this condition is now regarded as a cornerstone of preventive medicine.

The results of this epidemiological study show that the burden of 25-hydroxyvitamin D deficiency in a Mediterranean country without policy of food for-

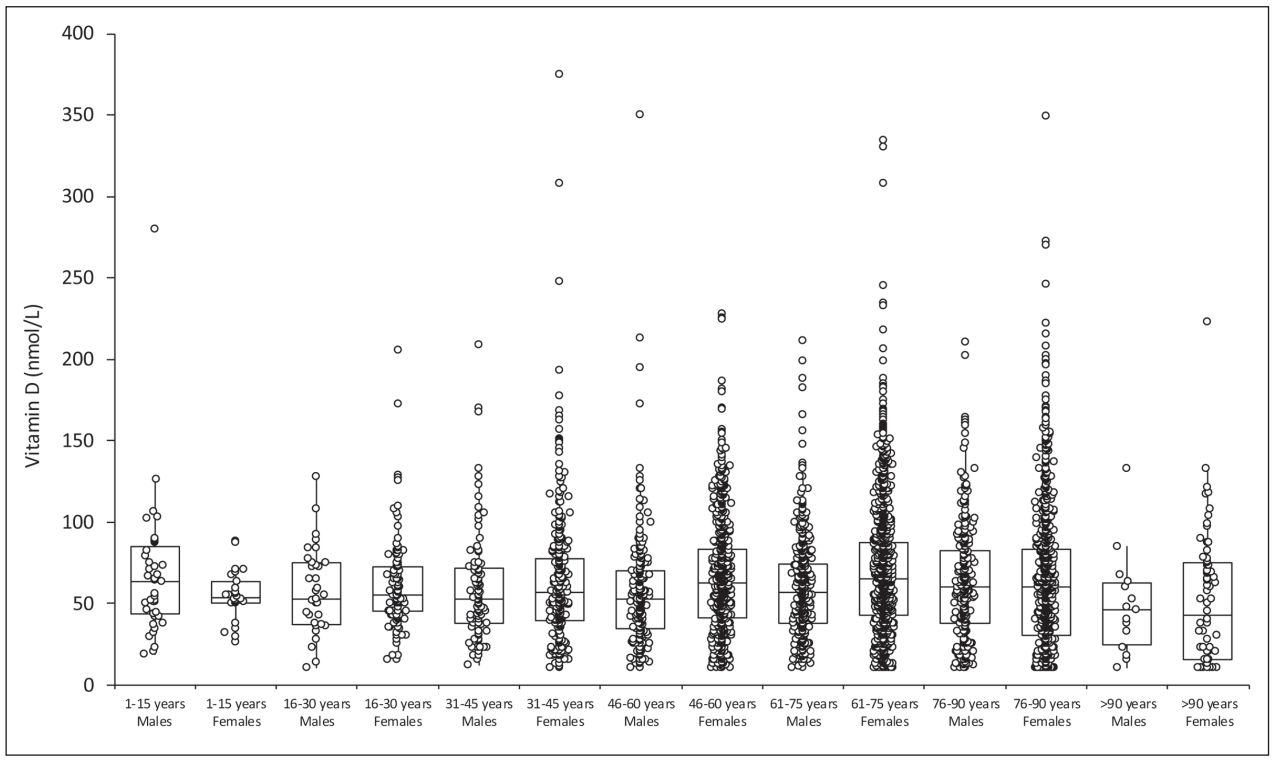

Figure 1. Distribution of vitamin D according to age and gender in a Mediterranean country without a policy of food fortification

tification is as high as 36%, thus exhibiting a further significant increase compared to the prevalence reported in a previous epidemiological study carried out between the years 2008 and 2011 in one of these two centers (i.e., 33%; p=0.001) (8). This probably reflects an ongoing trend of lower time spent in outdoor leisure activities in our country (9). Even more importantly, we also found that the rate of 25-hydroxyvitamin D deficiency was higher in men than in women, and that the prevalence varied significantly across ages, with a consistent trend towards increase in the elderly, especially in females. Interestingly, the burden of 25-hydroxyvitamin D deficiency was found to be more than double in subjects older than 90 years than in children (26% versus 53%; p<0.001).

Taken together, these findings may have at least two meaningful implications. First, the high and constantly increasing burden of 25-hydroxyvitamin D deficiency observed in our population raises the question as to whether a regional (or national) policy of food fortification may be advisable in the Mediterranean area, since similar epidemiological data were reported for other neighboring countries (3). It is also noteworthy that De Rui et al recently showed that regular enrolment in activities such as cycling and gardening was effective to limit the likelihood of inadequate vitamin D status in a population of the Progetto Veneto Anziani (9). As a complementary measure, therefore, promotion of outdoor activity should also be considered to increase 25-hydroxyvitamin D and support personal health and fitness.

The revision of the reference ranges of total serum vitamin D may be a second, important issue. Most of the studies that have attempted to define the reference range of 25-hydroxyvitamin D in the healthy adult population were carried out more than a decade ago. The life expectancy has constantly increased (by approximately 3 years) in the past decade in most western countries (10), as well as in our regions (11). This trend may have contributed to further increase the burden of 25-hydroxyvitamin D-deficient subjects in the general population. It is also noteworthy that a complex interplay exists between vitamin D metabolism and calcium, phosphate or parathyroid hormone (PTH),

so that the concentration of these parameters should be taken into account when establishing the potential cause of vitamin D deficiency in the single patient. Therefore, a local definition of reference ranges according to demographical and lifestyle characteristics of the resident population should be pursued.

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