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Vitamin D status and COVID-19 prevention in a worker subgroup in Italy

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Abstract.
BACKGROUND: Low levels of vitamin D are widespread in the world's population and associated with sun exposure, genetics, and lifestyles. Office workers in different occupational sectors seem more vulnerable than others. Scientific evidence reports a contribution of vitamin D in resistance to infections, opening to supplementation as a preventive action against pathogens, including SARS-CoV-2.
OBJECTIVE: A pilot campaign in the workplace during the coronavirus 2019 (COVID-19) pandemic was conducted based on the preliminary measurement of vitamin D amount and its integration.
METHODS: A preventive action to contrast the deficiency of vitamin D was offered to a population of 700 bank employees. Vitamin D supplementation was performed between April and June 2021, on workers ($n = 139$) and showed 25(OH)D serum levels ≤ 30 ng/ml. Demographic, anthropometric and lifestyle information were collected by survey and changes in the serum 25(OH)D amounts were monitored.
RESULTS: The adherence of the target population to the prevention campaign was 21%. 75% of the enrolled workers had low levels of vitamin D. After the intervention, serum vitamin D levels increased (1.28-fold; $p = 0.0001$) and 80% of the subjects reported optimal values > 30 ng/ml. Only 2.9% reported slight flu-like symptoms, but only 0.7% was confirmed as COVID-19, with respect to a ten-fold higher incidence in the general population.
CONCLUSIONS: Vitamin D supplementation can be achieved by simple and noninvasive approaches and can bring along further insights into health literacy on diet and lifestyles, representing an opportunity to protect the population by the widespread state of vitamin deficiency.

Keywords: Diet, nutrition, supplementation, health promotion, public health, cholecalciferol

1. Introduction

Vitamin D is a fat-soluble vitamin implicating in regulation of calcium metabolism and in the response of immune system [1–5]. To achieve these health benefits, the level of serum 25-hydroxyvitamin D should be > 30 ng/mL (75 nmol/L) [5–7]. This amount is principally achieved by cutaneous synthesis from sunlight exposure or by diet as consumption of fish [8–10]. However, serum vitamin D amount is due to several factors including environmental variables, such as latitude or season, and personal conditions, such as gender, age, race, adiposity, physical activity, dietary habits, and occupation [11–15]. The

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Table 1
Examples of different types of indoor workers and vitamin D amount in serum

Type of indoor worker	25-(OH)D Mean (ng/ml)	References
Administration workers	18.3	[22]
Banker and call center employees	24.9	[23]
Garment factory workers	14.7	[24]
Indoor daytime workers	19.9	[25]
Industry and civil service workers	23	[26]
Laboratory staff	17.6	[27]
Manager employees	16.2	[28]
Manufacturing workers	9.0	[29]
Shift workers at an engineering factory	13.4	[30]
University workers	7.6	[31]
Indoor athletes	15.3	[32]

elderly, hospitalized, patients and indoor employees are between susceptible groups for receiving a low exposure to sunshine, and at a risk for vitamin D deficiency [16–19]. Several studies (Table 1) show that workers in offices or indoor environments are more likely to develop hypovitaminosis D [18–32].

Although several studies report that no increase in vitamin D deficiency was described during and after the lockdown period, scientific attention was directed to evaluate strategies for coronavirus 2019 (COVID-19) prevention and vitamin D reinforcement in workers [33–38]. Most of the studies are limited to the categories on the forefront for the pandemic emergency, such as healthcare or military employees [33, 39–42]. However, several other work categories were not studied or involved in supplementation campaigns, even if undergoing insufficiency of vitamin D (Table 1) and being exposed for occupational reasons due to SARS-CoV-2, Orthomyxovirus or other pathogens. Workers employed in the tertiary sector may represent the groups with lowest vitamin D levels, including university personnel, but also different factory workers show low serum levels. However, the question of a deficiency of vitamin D is representative of a complex lifestyle situation [6–8]. Therefore, it should be approached as a component in wider health promotion strategies and independently from the COVID-19 pandemic, since it was also associated with other health risks [39, 43, 44]. The workplace represents a privileged opportunity for prevention campaigns [45]. The pandemic imposed the enforcement of preventive measures, requiring procedures and personal protective devices, but also strategies to empower and make workers aware. Here, vitamin D integration is recommended also as a flywheel opportunity for health promotion campaigns in the workplace, involving alphabetization to healthy lifestyles and prevention of COVID-19. Changes in serum 25(OH)D amounts were examined in a worker sub-group of bank employees, after daily 2000-IU vitamin D intake for three months. The final aim was to approach the daily intake of vitamin D3, in people potentially exposed to SARS-CoV-2, suggesting a model for supplementation in the workplace.

2. Materials and methods

2.1. Study design

Flow chart in Fig. 1 summarizes the study design. Briefly, the campaign was offered in February 2021 and supplementation carried on between April 2021-June 2021, a sample group of workers potentially exposed to SARS-CoV-2 joined the supplementation and follow up. All employees and collaborators of a banking institute ($n = 700$) were invited on a voluntary basis in the health promotion campaign to enforce their levels of vitamin D. This action was part of a larger campaign focused to strengthen the defenses against COVID-19 by improving health literacy and enforcing current safety procedures. Meetings, documentation, and information leaflets were provided, following standard national guidelines [46, 47]. The 22% ($n = 154$) joined the supplementation action. Finally, 139 subjects were enrolled after fulfilling the inclusion/exclusion criteria, mainly: 25(OH)D serum levels ≤ 30 ng/ml, no pregnant status, no use of immunosuppressive or antiviral drugs. The data collection procedures used in this study complied with the ethical requirements of the official committees, the 1964 Helsinki Declaration, and its modifications. Prior informed consents were obtained from all participants and data confidentiality and anonymity were strictly maintained. Epidemiological research was evaluated and authorized by the IRC (Internal Research Committee) of the University of "Foro Italico" in Rome (n. CAR 31/2021).

2.2. Intervention campaign

In collaboration with the administrative management and the occupational health section an integrated preventive campaign was offered to 700 employees of the Bank to verify vitamin D levels and provide supplementation when required (Fig. 1). This action was performed during a COVID-19 pandemic

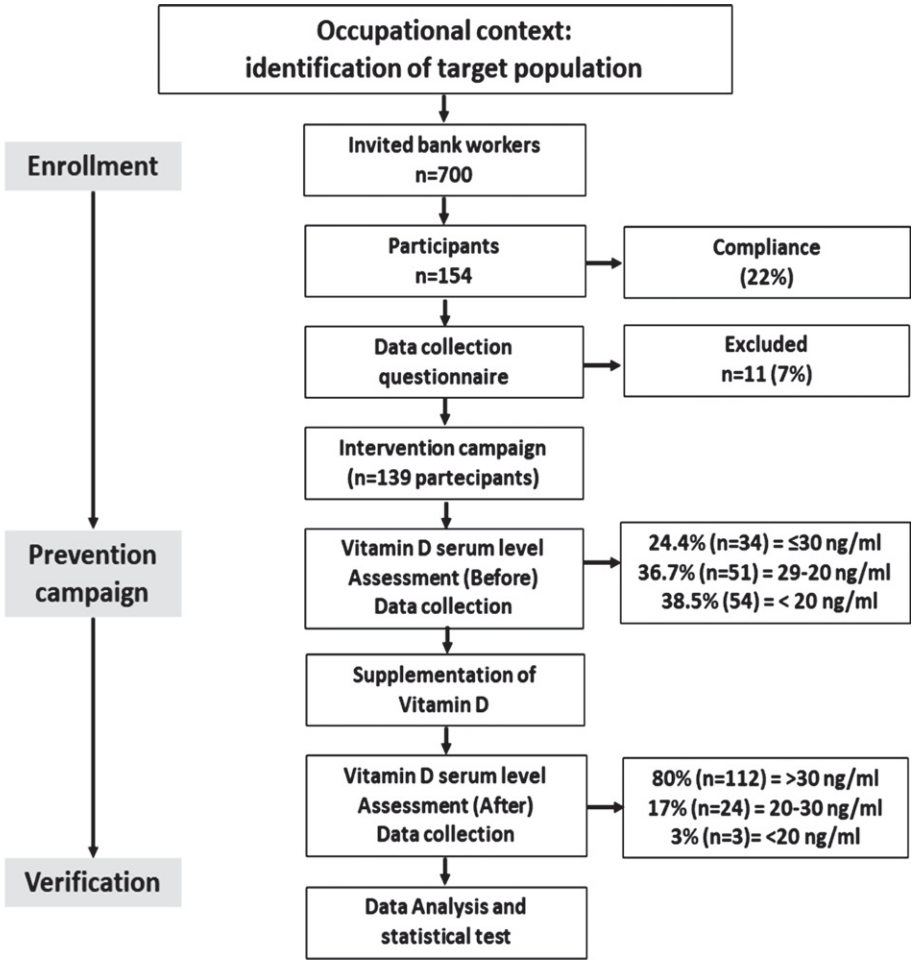

Fig. 1. Flowchart: Description of the study design.

peak and flanked by basic information on SARS-CoV-2 (alphabetization) and documentation on safe behaviors and preventive procedures in the workplace (health education). Among all recipients, a subgroup ($n = 154$) was enrolled, filled out the questionnaire and underwent assessment of vitamin D levels. Based on inclusion/exclusion criteria a final group of 139 workers has taken 2,000 IU of vitamin D3 - Cholecalciferol (Dekoro, Named, Italy) every day at breakfast for 12 weeks. The self-administration was taking place directly in the oropharynx through three sprays of an oral solution in the form of nano-droplets.

2.3. *Questionnaire*

A structured, anonymous, and voluntary questionnaire comprising two sections was considered to acquire data on the enrolled population sample and reduce the interference of major confounders. The first section focused on socio-demographic information: gender, age, nationality, and educational level. Additional information included: weigh, height, smoking habit (yes/no), eating habits (diet and intake of fish-based meals), alcohol consumption (yes/no), level of exercise (none, sporadic and often), and sports activities (indoor, outdoor, or blended) or sunlight exposure (1 = as soon as possible I expose myself to the sun; 2 = I often expose myself ->5 hours per day; 3 = rarely - less than an hour a day; 4 = hardly ever/never). Moreover, specific questions were considered on conditions relative to exposure to SARS-CoV-2, symptomatology and/or positivity to COVID-19, disease severity (e.g. onset and/or admission to hospital or an intensive care unit). The survey was performed before and after the supplementation, collecting data up to six months (February 2022) after the intervention campaign.

Table 2
Main demographic and anthropometric features of workers and vitamin D serum levels before and after supplementation

Male sex, n (%)	43.0 (31)
Age, y, mean (SD)	47.2 (8.9)
Body mass index, kg/m^2, mean (SD)	24.4 (5.4)
Weight (kg), mean (SD)	72.2 (19.4)
Height (m), mean (SD)	1.7 (0.1)
Serum 25OHD, ng/mL, mean (SD) pre	21.2 (5.4)
Serum 25OHD, ng/mL, mean (SD) post	34 (10.3)
Variation Serum 25OHD (Δ)	12.8

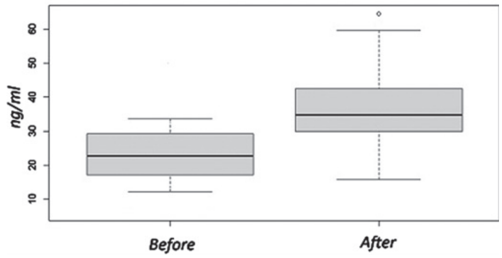

Fig. 2. Vitamin D dosages before and after supplementation.

2.4. Blood data

The 25(OH)D amount in blood were revealed by the standard enzyme immune-assay (Abbott, USA). The thresholds, identifying by the guidelines and scientific literature, were > 30 ng/mL, 20–30 ng/mL, and < 20 ng/mL and were defined as sufficiency, insufficiency, or deficiency of vitamin D, respectively [39, 44, 46, 47].

2.5. Statistical analysis

The student's t-test was used with continuous variables and to investigate categorical variables such as men and women, sport indoor and outdoor or blended, typologies of eat habits, the chi-squared test was performed. To estimate the relationship among serum vitamin D levels in worker population a simple correlation and regression analyses were performed. ANOVA (One-way) and linear regression test were used for evaluating variations in serum 25(OH)D levels. Multiple linear regression analyses were performed to comparison 25(OH)D status in blood and physical activities variables and considering age, body mass index (BMI), and type of exercise as confounding factors. BMI was estimated as weight [kg]/height [m^2] [48].

3. Results

Table 2 summarizes demographical data and serum levels of 25OHD pre and post campaign in the population sample. A nonsignificant difference between the participants was noticed for age (47.2 ± 8.9) and BMI (24.4 ± 5.4). The mean of vitamin D levels among workers was 21.2 ± 5.4 ng/mL (Table 2). Nonstatistical difference was reported between level of serum 25OHD and range of age. Thus, after the study, 3 months after intake, serum vitamin D levels showed a 1.28-fold ($p = 0.0001$) increase (Table 2, Figs. 1 and 2). Further, 80% of the subjects undergoing treatment reported a value > 30 ng/ml and 17% reported > 20 ng/ml and 3%<20 ng/ml.

Workers with graduate instruction showed higher serum 25(OH)D levels (22.1 ng/mL) than those with secondary education (19.3 ng/mL) or without a specialized education (11.1 ng/mL, $p = 0.001$). At the beginning of the survey only 24.4% of participants ($n = 34$) had values close to 30 ng/ml and 36.7% ($n = 51$) between 20 and 30 ng/ml, while 38.5% ($n = 54$) had values < 20 ng/ml.

In the women were found levels significantly higher of vitamin D both before (24.7 ± 5.3 vs. 20.8 ± 8.6, $p = 0.007$) and after (35.2 ± 7.8 vs. 34.9 ± 10.3, $p = 0.005$) (Fig. 3). Vitamin D dosages before and after (Fig. 4) in relation to the type of diet (frequency of fish consumption: 1 = no portions per week, 2 = 1-7 portions per week, 3=>7 portions per week) revealed contrasting results with a trend of vitamin D levels increasing with the fish-based dietary intake. However, this relationship was lost in those subjects declaring to eat more than seven fish-based meals (Fig. 4).

Sun exposure and vitamin D amount association was not consistent (Fig. 5). However, there is a significant variation between groups 3 and 1 ($p < 0.01$). The vitamin D intake through preventive campaign abolished the differences due to poor sun exposure and all group reached serum levels higher than 30 ng/ml (1 = 41 ng/ml, 2 = 30 ng/ml, 3 = 32 ng/ml, 4 = 32 ng/ml).

Regarding the frequency of SARS-CoV-2 diseases in the enrolled population, only 2.9% of subjects (4 out of 139) reported COVID-19 symptoms during and post the intervention, but only one was confirmed as a COVID-19 case. Therefore, the final incidence observed in the enrolled population was about 0.7% with respect to the incidence reported for general population (in that same Italian district during the

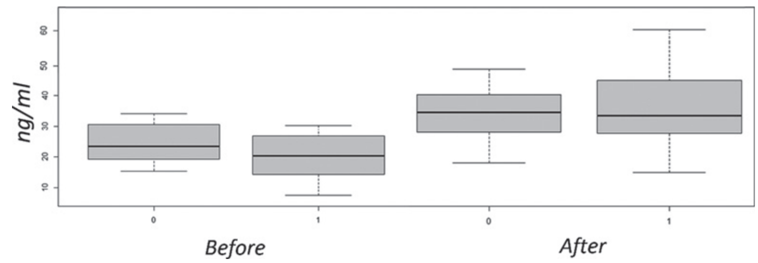

Fig. 3. Vitamin D dosages before and after treatment by gender (1 = male, 0 = female).

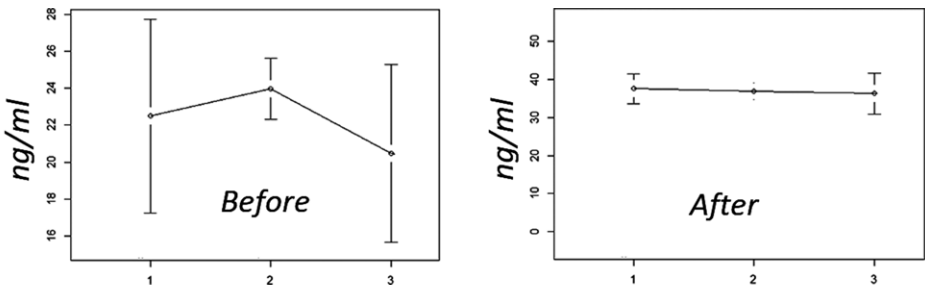

Fig. 4. Vitamin D dosages before and after in relation to the type of diet (frequency of fish consumption: 1 = no portions per week, 2 = 1-7 portions per week, 3=>7 portions per week).

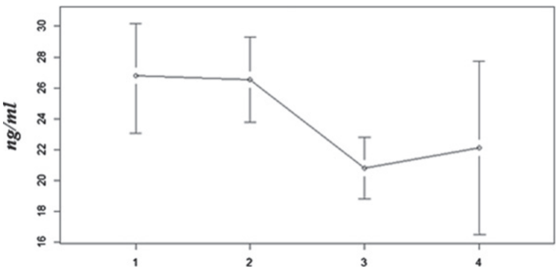

Fig. 5. Vitamin D dosages with respect to sun exposure: 1 = as soon as possible I expose myself to the sun; 2 = I often expose myself - more than 5 total hours per day; 3 = rarely - less than an hour a day; 4 = hardly ever/never.

same April-June period 2021) that was ranging from 7% to 9% [49]. Moreover, this subject was infected at the very beginning of the study, when having still deficient serum 25(OH)D amounts (11.3 ng/ml). Interestingly, two independent subjects underwent continuous exposure to SARS-CoV-2 from cohabiting children in their respective families, without subsequently becoming infected; both had already reached Vit D values > 30 ng/ml after the supplementation (47.5 ng/ml and 46.7 ng/ml, respectively). This surveillance on COVID-19 contagion was collected within the 3 months of the intervention campaign and prolonged in the following 6 months, up to February 2022.

4. Discussion

The global vitamin D deficiency has achieved an unexpected prevalence, as underlined in several life and occupational contexts also during the COVID-19 era. This trend has drawn significant concern to clarify the possible impact of vitamin D deficiency or insufficiency and to develop prevention strategies for reducing the associated risks, including susceptibility to infectious diseases [33–37]. Some workers, such as those employed in indoor environments, receive lower sunshine exposure, and can develop vitamin D inadequacy [17–32]. Among these, bank managers, office employees, call center operators and university workers represent subgroups of workers that were not studied during the COVID-19 pandemic, with respect to other categories such as militaries and hospital personnel [33–35, 40–42]. These workers are reported to be susceptible for both vitamin D deficiency and exposure to highly contagious respiratory pathogens, such as SARS-CoV-2 [49–52].

Here, a health promotion campaign was performed during a COVID-19 pandemic peak, in 2021. Basic information on SARS-CoV-2 transmission and presentations on safety procedures in the workplace were flanked by an intervention for vitamin D supplementation. Therefore, the proposed model joined three actions: health literacy by documentation and meetings, occupational prevention by enforcement of safety procedures, and reduction of vitamin D deficiency by integration. Vitamin D represents a valuable opportunity to provide health promotion not only for enhancing COVID prevention campaigns, but also for supporting healthy behaviors such as appropriate exposure to sunlight, diet, physical activity. Several evidences, indeed, support its benefits both versus infectious [10, 38, 47, 52] and non-communicable diseases [53], even if there is no agreement for other conditions, such as cancer or diabetes [54]. Furthermore, even if different context can harbor health literacy and health promotion actions, the workplace represents an effective and privileged opportunity [45, 56].

The study was carried out on bank employees, representative of indoor workers, at risk for lower sunlight exposure, sedentary habits, contact with the public and COVID-19 contagion. Changes in the serum 25(OH)D quantities, after intake 2000-IU vitamin D for three months and health status for six months, were monitored. Before the intervention, vitamin D levels in most of all participants were found to fall well below the levels reported as ideal for health [39, 44, 46, 47]. Age and gender were indicated as significant predictor factors of low levels of vitamin D in populations working in indoor office [57, 58]. However, here, a vitamin D deficiency was observed in all age ranges examined before the intervention suggesting the vulnerability of the bank employees to vitamin D insufficiency, regardless of age. This interestingly finding supports some recent studies showing a tendency to hypovitaminosis D among younger workers [58]. Some possible explanations include the inclination of the younger generation of workers to stay indoors due to the exponential increase in the utilization of computer technologies both for working and hobby, especially in the COVID-19 era. This was exacerbated by the lockdown measures but is also linked to different lifestyles. Additionally, a lower intake of vitamin D (<5%) was reported among younger workers compared to older ones (20%) [57, 58].

Unexpectedly, here, variations between vitamin D serum levels in people who practice physical activity indoor, or outdoor did not show to be significant. This could be due to the limited sample size and/or several different reasons including the dissimilarity in the time of exposure to sunlight during sport or physical activities; indeed, the percent conversion to pre-vitamin D3 from 7-dehydrocholesterol (7-DHC) and its photoproducts is maximum in the central hours of the day during the entire year [58]. However, identifying the best exposure must consider several parameters, comprising climate, weather conditions, location, air pollution, and the surface of the exposed body area [58–61]. In this case, although exposure time was not significantly related to vitamin D amount, the difference between subjects frequently exposed to sunlight and those who expose rarely was significant, suggesting the positive impact to promote outdoor activities or to increase opportunities for safe exposure to sunlight, even considering work-time breaks [61, 62].

In the women significantly higher vitamin D levels were found both before (24.7 ± 5.3 vs. 20.8 ± 8.6, $p = 0.007$) and after (35.2 ± 7.8 vs. 34.9 ± 10.3, $p = 0.005$). This result is not in accordance with other studies showing a lower vitamin D level in women [63, 64]. However, most of these studies focused on a gender evaluation involving women beyond menopause, which is known to be an age at risk for vitamin D deficiency, while in the present study the mean age was lower, and about 47.2 (38.3-56.1) years. Epidemiological reports in several populations have showed how vitamin D deficiency is frequent in women after menopausal compared to young women [65, 66].

Regarding participants with graduate education the serum 25(OH)D amount was higher (22.1 ng/ml) than those with secondary instruction (19.3 ng/mL) or deprived of specialized education (11.1 ng/ml, $p = 0.001$). This finding agrees with other reports, describing that among sociodemographic factors, affecting the vitamin D deficiency, there are inadequate environments, weak economic conditions, and minimum level of education [67].

Regarding diet, contradictory results show an increasing trend of vitamin D levels linked to fish-based dietary intake but inverted when subject declare to eat > 7 fish-based meals. These results showed the variations in food consumption among workers and the difficulty to control this variability due to subjective elements [68, 69]. Thus, a public health strategy to enhance the dietary intake of vitamin D among indoor workers, could likely be a combination of a healthy nutrition promotion and supplementation [69]. Nowadays, the availability of diffused serum tests for evaluating vitamin D levels, may be an additional support to evaluate deficiencies, avoid overdose, monitor efficacy of diet supplementation.

To the best of our knowledge, this is the first interventional study among office employees, and in particular bank workers. This prevention campaign was positively accepted representing an opportunity to facilitate communication and awareness during a stressing period dominated by COVID-19 concerns in the workplace. The proposed supplementation plan was adequate, achieving optimal circulating levels, by an easy administration by spray, that was largely appreciated by the participants. No toxic effect or excessive levels of vitamin D were detected at the end of the supplementation period. Before the study only 24.8% of the population showed vitamin D serum values equal to 30 ng/ml and 36.7% between 20 and 30 ng/ml, while 38.5% had deficiency values < 20 ng/ml. After the 3 months supplementation period, the increase in serum vitamin D levels improved 1.28-fold ($p = 0.0001$). The 80% of the subjects reported values > 30 ng/ml even if a remaining 17% had still insufficient levels slightly below the 20 ng/ml. In the current study, 25(OH)D supplementation was related to reduction of risk of developing symptomatic COVID-19. Only 3.9% of participants reported COVID symptoms in the last 3 months but only one was confirmed as a COVID-19 case (0,7%), while in the same period the incidence in the general population of that area was ranging between 7% and 9%. Anyway, vitamin D is supposed to enforce resistance to infections and modulate the immune system, whereas its deficiency was linked with enhanced frequency of airborne infections, including COVID-19 [38, 70–72].

The potential usefulness of vitamin D in preventing respiratory diseases was suggested by several previous studies, but the effectiveness and appropriateness in COVID-19 prevention in the workplace remains to be elucidated by larger randomized control trials. Indeed, this pilot study intend just to propose a model and has several limitations. First, people involved in the study were restricted to a small number of banker workers and this can be unrepresentative of all indoor workers. Moreover, the population involved still oscillated between smart-working and face-to-face work and this aspect have affected the level of responses reported (22%). Second, potential bias or confounders might still be found and should be clarified through future studies with longer follow up and more extended sample size, such as the seniority of job title or the smart working condition. Third, the study design is fewer strong than a randomized controlled trial and was not projected in a population that receives a vitamin D placebo. A larger and randomized study should have to consider several further indoor workers categories, additional strategies for collecting environmental and lifestyle data, to propose guidelines or suggest the prevention strategies for vitamin D inadequacy in the workplace, with or without COVID-19. Moreover, the extension of similar health promotion intervention is recommended also to examine and improve the effect of stakeholder involvement, organization culture, physical and social environments in promoting the daily intake of vitamin D3, in a One Health perspective.

5. Conclusions

The supplementation with vitamin D represents a useful, available, and well-tolerated auxiliary treatment for COVID-19. Although the sample size considered is relatively small compared to what could be obtained from a larger epidemiological survey, and although therefore conclusions emerging from this limited sample should be taken with caution, insights supporting a favorable association among improved vitamin D levels and protection from COVID-19 do emerge in bank employees. Considering other studies and a recent systematic literature review, this association appears plausible and reinforces the case for continuing and extending this preventive strategy. Indeed, the totality of these observations supports the achievement of the prevention goals proposed by the study, both in terms of achieving optimal vitamin D values in a relatively short time and in light of the contingent situation related to protection with respect to the epidemiological emergence from COVID-19. Any supplementation campaign may further represent a valuable opportunity to flank health literacy and health promotion actions in the workplace.

Ethical approval

The epidemiological research was evaluated and authorized by the IRC (Internal Research Committee) of the University of “Foro Italico” in Rome (n. CAR 31/2021).

Informed consent

Informed consent was obtained from all participants prior to enrollment. Data confidentiality and anonymity were strictly maintained.

Conflict of interest

None of the authors declare any commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement) that might pose a conflict of interest in connection with the submitted article.

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