Rotating shift workers with vitamin D deficiency have a higher risk of obstructive sleep apnea

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Abstract
Objectives The study aimed to evaluate the association between obstructive sleep apnea (OSA) and vitamin D deficiency (VDD) in shift workers.

Methods This cross-sectional study included male rotating shift workers in an iron ore extraction company. Participants were classified as VDD when 25(OH)D < 20 ng/mL for a healthy population and 25(OH)D < 30 ng/mL for groups at risk for VDD. Risk of developing OSA was classified by Berlin questionnaire (BQ) and NoSAS score. Data were compared using chi-square analysis with Cramer’s V as effect size, and Bonferroni correction. Multivariate logistic regression analysis was performed to investigate whether or not VDD was associated with OSA risk assessment.

Results Among 1423 male workers, mostly younger, aged 30 to 39 years (53%), worked shifts for more than 5 years (76%). The prevalence of high risk of OSA by BQ was 16%, and 33% by NoSAS score. Additionally, 29% had VDD. In multivariate analysis, controlled for confounding factors, workers with VDD had a 52% increased chance of OSA by BQ (OR 1.52; CI95% 1.06–2.18) and a 64% increased chance of OSA by NoSAS score (OR 1.64; CI95% 1.09–2.48). After subgroup analyses, similar results were not observed in workers aged 20–29 and 30–39 years.

Conclusion Rotating shift workers with vitamin D deficiency are more likely to have obstructive sleep apnea, assessed by the Berlin questionnaire and NoSAS score.

Keywords Obesity · Circadian rhythm · Sleep apnea syndromes · Workers · Young adults

Introduction

Obstructive sleep apnea (OSA) is a common sleep problem in adults of all age groups [1]. It is related to a variety of health-related consequences, including increased risk of cognitive impairment, depression, metabolic disorders, hypertension, cardiovascular disease, atrial fibrillation, and mortality [2, 3]. Population studies show that the prevalence of OSA in the general population reaches more than 30% of the population and almost 50% in men [1, 4]. The estimated global prevalence of obstructive sleep apnea is that about 900 million adults have some degree of OSA [5].

As a result of airway collapse, hypoxia, and sleep fragmentation, individuals with OSA have increased activation of the sympathetic nervous system during sleep, which leads to daytime sleepiness, increased heart rate, arrhythmias, awakenings, and other clinical manifestations [6].
The prevalence of OSA can be as high as 90% in some groups [7], can vary according to gender, age, and associated comorbidities [8]. In addition, previous studies have hypothesized that OSA might have a higher incidence and severity in winter [8]. From this, it was considered that there might be some relationship between OSA and vitamin D deficiency (VDD), which is more prevalent in periods of low sunlight [9].

This hypothesis has been supported by recent studies showing that decreased vitamin D levels and sleep disturbances are associated in different populations [10–13]. The possible mediating or causal effects of vitamin D deficiency in sleep apnea are related to the accumulation of adipose tissue and muscle decline caused by VDD, increasing the chances of airway obstruction during sleep [13, 14]. And it may also be related to higher pro-inflammatory states and is commonly associated with OSA [15]. And finally, studies show that VDD can increase circulating prostaglandin D2, increasing sleep complaints and problems [16, 17]. All of these elements are reported to be involved in the pathophysiology of OSA.

These hypotheses were corroborated by other studies in the literature that demonstrate decreasing in vitamin D with increasing severity in OSA [18–22]. Furthermore, Liguori et al. (2015) demonstrated that the commonly used therapy for OSA, continuous positive airway pressure (CPAP) therapy, can increase vitamin D levels in patients with OSA [14].

Epidemiological studies have shown that certain groups of individuals or populations are at the same time more susceptible to both sleep disorders and VDD, for example, individuals with obesity [23], afro-descendants [24], and also certain occupations and work shifts [25–27]. The alternating shift workers are a group at risk for both situations. Vitamin D deficiency is identified in up to 80% of alternating shift workers [25], and alterations in sleep architecture are common in these workers since this work schedule leads to changes in circadian rhythm, daily routine, and hormonal changes [28].

However, to our knowledge, there is no study evaluating how vitamin D deficiency is associated with sleep apnea in shift workers. Therefore, this study aimed to verify the association of vitamin D deficiency with OSA evaluated by the Berlin questionnaire and NoSAS score in alternating shift workers.

Methodology

Design and participants

The current study was conducted with a population of shift workers from an iron ore extraction company in Brazil, at Minas Gerais and Pará. Three cross-sectional studies were conducted, and the population of shift workers with the position of operators was invited to participate: (a) The first was carried out in 2012, with 337 shifts workers from four mines in the Iron Quadrangle region; (b) the second study was carried out in 2015 with 192 shifts workers from another mine in the Iron Quadrangle region; (c) the third study was carried out in 2018 with 932 shifts workers in the southern region of Pará [29]. Therefore, in total, 1461 shift workers were evaluated. Of these only 38 were women (3%). For this study, we considered only men (n = 1423). The Strengthening Reporting of Observational Studies in Epidemiology (STROBE) guidelines were used in the design and construction of the study.

The workers had two types of alternating shifts, as follows: (a) In Minas Gerais, the workers had rotating shifts of four days worked and one day off, in this way they worked for six hours, followed by 12 h rest. After finishing the weekly four-shift cycle, they received one day off. (b) In Pará, the workers had a rotating shift of 5 days worked and 2 days off, so they worked for eight hours followed by 24 h rest. After finishing the five-shift weekly cycle, they received 2 days off.

Data collect

In all studies, data collection was performed face-to-face by teams trained to administer the questionnaires, measure anthropometric data, and collect biological samples.

Sociodemographic variables (sex, age, skin color, education, and shift schedule) were assessed. Age was categorized into age groups (20–29; 30–39; 40–49; 50–59, and 60 years or older); skin color was self-reported and grouped as non-white (black, brown, yellow, or indigenous) and white; education was categorized according to the degree of schooling (1st-degree completed, 2nd-degree completed, technical, graduate, and postgraduate); and shift work time was grouped into ranges (< 5 years and ≥ 5 years).

The clinical evaluation was carried out employing a questionnaire about pre-existing diseases, use of medication, smoking, alcohol consumption, physical activity; and measuring blood pressure. The Alcohol Use Disorders Identification Test (AUDIT) was used to evaluate alcohol use dependence [30]. Individuals who reported that they had never smoked, or quit smoking more than 6 months ago, were classified as nonsmokers, and individuals who reported that they currently smoke or quit smoking less than six months ago were classified as smokers. Furthermore, the Fagerström Test for Nicotine Dependence (FTND) was used to evaluate nicotine dependence; 6 questions are used to produce a score from 0 to 10 points [31]. For analysis purposes, participants with no risk and low risk were grouped into the same category (AUDIT 0–7 points; FTND: 0–5 points). The International Physical Activity Questionnaire (IPAQ)
was used to assess the level of physical activity of the study individuals. The workers were classified as low physical activity <600 measure total energy (MET)—min/week [32]. The pre-existing diseases evaluated were: cardiovascular diseases, respiratory diseases, and chronic kidney disease. To evaluate hypertension, the workers’ blood pressure was measured with a semi-automatic digital device in triplicate. The measurement protocol followed the recommendations of the Brazilian Society of Cardiology, and workers who had systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg were classified as having hypertension [33].

### Biochemical data

The evaluation of the biochemical profile was performed by analysis of the lipid profile, vitamin D, and glycemic. In the first two studies (2012 and 2015), blood samples were collected after a 10-h fast and in 2018 it was collected without a previous fast.

The lipid profile of the workers was determined by the enzymatic colorimetric method. Low-density lipoprotein cholesterol (LDL) was calculated using the Friedewald Eq. (1972), by the formula: total cholesterol —[(HDL + (triglycerides/5)]. The total cholesterol (TC) was classified as normal < 190 mg/dL, HDL > 40 mg/dL, LDL < 130 mg/dL, and triglycerides (TG) < 150 mg/dL with fasting and < 175 mg/dL without fasting [34]. Dyslipidemia is classified when at least one of the parameters was altered or uses lipid-lowering drugs. Glycemic index was evaluated by fasting plasma glucose (FPG) in Minas Gerais, and glycosylated hemoglobin (HbA1c) in Pará. Workers were classified as hyperglycemic with FPG values ≥ 100 mg/dL or HbA1c ≥ 5.7% [35]. Vitamin D was determined by the chemiluminescence method and classified as deficiency 25(OH)D < 20 ng/mL to a healthy population and 25(OH)D ≤ 30 ng/mL for groups at risk for VDD (body mass index ≥ 30 kg/m², age ≥ 60 years, and presence of chronic kidney diseases) [36]. The seasonality of blood sample collection was classified as either autumn (March 20 to June 20), winter (June 21 to September 23), spring (September 21 to December 20), or summer (December 21 to March 19).

### Anthropometric data

To evaluate body adiposity, we used a general adiposity indicator, the body mass index (BMI), and two indices of peripheral adiposity, waist circumference (WC), and neck circumference (NC). Height was measured using a stadiometer with a scale in centimeters and accuracy of 1 cm. Weight was measured on a portable body composition monitor. BMI was calculated and classified according to the World Health Organization (WHO) as eutrophic (BMI 18.5–24.9 kg/m²), overweight (BMI 25.0–29.9 kg/m²), and obesity (BMI ≥ 30.0 kg/m²) [37]. WC was measured, in triplicate, with a simple and inelastic measuring tape at the midpoint between the iliac crest and the last costal arch, and classified as central obesity values ≥ 90 cm [38]. NC was measured at the level of the cartilage, just above the laryngeal prominence, and classified as increased values ≥ 40 cm [39].

### NoSAS score

The NoSAS score was calculated according to Marti-Soler et al. (2016), ranging from 0 (low risk for OSA) to 17 points (highest risk for OSA): NC ≥ 40 cm, 4 points; BMI 25–29 kg/m² and BMI ≥ 30 kg/m², 3 and 5 points, respectively; the presence of snoring, 2 points; age ≥ 55 years, 4 points; and male sex, 2 points. The cut-off point for high-risk classification for OSA was ≥ 8 points [39].

### Berlin questionnaire

The Berlin questionnaire adapted and validated for Brazil [40] was applied to all workers. The BQ has three categories: witnessed snoring and apnea, excessive daytime sleepiness, and OSA-related comorbidities. The cut-off point for high-risk classification for OSA was two positive [40].

### Statistical analysis

The Stata program (version 15.0) was used to assist the statistical analyses, considering an alpha of 5%. Pearson’s chi-square with Bonferroni correction was performed to verify the difference between the groups. Cramer’s V was used for Chi-squared analyses as an effect size, with the thresholds 0.10 (small), 0.30 (medium), and 0.50 (large).

To investigate whether VDD was associated with risk for OSA, we performed multivariate logistic regression from a hierarchical model of determination. This type of analysis considers the association of each variable with the outcome, controlling for possible confounder effects between proximal and distal variables. We developed our conceptual model to integrate sociodemographic, clinical, and anthropometric factors to explain their relations of OSA with VDD. Adjusted model 1 included seasonality, age, years of shift work, scholarly, skin color, and geographic location; model 2 adjusted by model 1 in addition to hyperglycemia, dyslipidemia, and hypertension; and model 3 was adjusted by the variables from model 2 in addition to adiposity variables, body mass index, waist circumference, and neck circumference. Collinearity among the covariates was evaluated. Hosmer–Lemeshow test and Akaike information criterion (AIC) were used to assess the goodness-of-fit of the models.

Using the program G*Power (version 3.1.9.2), we evaluated the a posteriori sampling power. We considered an
alpha level of 0.05 (using a two-tailed test) and estimated a sample power of 0.98.

**Ethical issues**

This study was approved by the Research Ethics Committee of the Federal University of Ouro Preto (2012: CAAE: 0018.0.238.00–11; 2015 CAAE: 39,682.014.7.0000.5150; 2018: CAAE: 93,760.618.5.0000.5150), and followed all the guidelines of the Helsinki Declaration. Written informed consent was obtained from all participants.

**Results**

The study included 1423 male rotating shift workers from two different mining regions in Brazil, and 29% had VDD, with a median 25(OH)D of 26.3 ng/mL, a minimum of 5.0 ng/mL, and a maximum of 65.7 ng/mL. Most workers were younger, aged 30 to 39 years (53%), with a minimum of 20 and maximum of 65 years, 73% self-reported as non-white, had up to 2nd-degree complete (72%), and worked shifts for more than 5 years (76%). Regarding anthropometric, clinical, and behavioral variables, most workers had high WC (63%), 39% had high NC, 78% had dyslipidemia, almost half had a low level of physical activity (49%), and 2% had medium and high-risk nicotine consumption by Fagerstrom test, and 10% had medium and high-risk alcohol consumption by AUDIT (Table 1).

The elevated risk for OSA among alternating shift workers was 16 to 33%, considering the BQ and NoSAS score, respectively. Besides, workers with VDD had a higher prevalence of OSA (p < 0.001) (Table 1).

Workers with VDD had a higher prevalence of BQ categories 1 (snoring) and 3 (comorbidities) when compared to workers without VDD (p < 0.001). Category 2 (excessive daytime sleepiness) had the lowest percentage of positive scores (5%). For the NoSAS score, workers with VDD had high positive criteria for overweight, obesity, high NC, and the presence of snoring (p < 0.001) (Table 2).

When we evaluated the association of VDD with OSA in multivariate analysis, controlled for all confounding factors (model 3), workers with VDD were 52% more likely to be at high risk for OSA, measured by BQ (OR 1.52; CI95% 1.06–2.18) and 64% increased chance of high risk for OSA from NoSAS score (OR 1.64; CI95% 1.09–2.48) (Table 3).

We also evaluated the association of VDD with risk for OSA stratified by age groups. In workers 40 and older, those with VDD had a 69% and 109% increased chance of high risk for OSA, on BQ and NoSAS, respectively (Table 4).

**Discussion**

This is the first study of male rotating shift workers in an iron ore mining company to examine the association of VDD and OSA risk. Our findings showed that shift workers who were vitamin D deficient were at higher risk of obstructive sleep apnea, as evaluated by the Berlin questionnaire and NoSAS score.

We found that 29% of the workers evaluated had VDD, and was more prevalent in workers older than 40 years, with longer working time in rotating shifts, high WC and NC, with chronic diseases, and in workers at high risk for OSA. The shift workers evaluated had vitamin D deficiency similar to that found in the general population of Brazil, which was 33% [41]. However, below the prevalence found in a systematic review study by Sowah et al. (2017), in which up to 80% of rotating shift workers have VDD [25]. Furthermore, Coppeta et al. (2018) in their systematic review found that of the occupations evaluated, shift workers and indoor workers are at high risk of having vitamin D deficiency [27]. Among the hypotheses of this risk factor, studies show that internal and alternating shift workers may be less exposed to sunlight due to occupational characteristics, leading to lower vitamin D synthesis in the epidermis [25]. The lower prevalence of VDD in our study may be partially explained due to the workday, where the work schedule provides periods of day shift, or on their days off from work, in which the individual can perform outdoor activities, with greater exposure to the sun.

We also found that 16% and 33% of workers were classified as high risk for OSA by BQ and NoSAS, respectively. And it was almost twice as high in workers with VDD, with 30% and 61% at high risk for OSA by BQ and NoSAS. The gold standard for diagnosing OSA, polysomnography, is not accessible to the entire population of shift workers. Therefore, it is estimated that about 80% of individuals are not correctly diagnosed with OSA [42]. Thus, alternative, more accessible, and simplified instruments, have been used in the screening of OSA [43, 44] and perhaps be of interest in rotating shift workers and other individuals at high risk for OSA [45].

Recent studies have shown that 1 to 4 people in the general population are at high risk for OSA, depending on gender, age, and diagnostic method used [7, 39]. Two large population-based cohorts, the HypnoLaus and EPISONO, entered that the high risk of OSA measured by the BQ ranged from 25 to 30%, and when assessed by the NoSAS score ranged from 35 and 43% [39]. In both studies, the prevalence measured by the BQ was at least two times higher than that found in our study. This difference may be related to the age of the participants, in which 43% of the subjects assessed were 60 years or older, an age group different from...
Table 1 Characteristics of rotating shift workers, total and by vitamin D deficiency

| Characteristics                        | Total (n = 1423) | Vitamin D Normal (71% (n = 1009)) | Deficient (29% (n = 414)) | p    | V  |
|----------------------------------------|-----------------|-----------------------------------|---------------------------|------|----|
| Vitamin D, ng/mL                       | 26.3 (10)       | 29.2 (10)                         | 19.1 (5)                  | <0.001 | -  |
| Age                                    |                 |                                   |                           |      |    |
| Years                                  |                 |                                   |                           |      |    |
| 20–29 years                            | 35.3 (10)       | 35.0 (9)                          | 37.0 (10)                 | <0.001 | -  |
| 30–39 years                            | 759 (53)        | 552 (55)                          | 207 (50)                  |       |    |
| ≥ 40 years                             | 442 (31)        | 289 (29)                          | 153 (37)                  |       |    |
| Skin color                             |                 |                                   |                           |      |    |
| White                                  | 386 (27)        | 285 (28)                          | 97 (26)                   | 0.122 | 0.054 |
| Not white                              | 1037 (73)       | 724 (72)                          | 317 (77)                  |       |    |
| Scholarly                              |                 |                                   |                           |      |    |
| 1st-degree complete                    | 55 (4)          | 34 (3)                            | 21 (5)                    | **0.010** | 0.089 |
| 2nd-degree complete                    | 1017 (72)       | 717 (71)                          | 300 (73)                  |       |    |
| Technician                             | 320 (23)        | 242 (24)                          | 78 (19)                   |       |    |
| Graduated                              | 31 (2)          | 16 (2)                            | 15 (4)                    |       |    |
| Shift work                             |                 |                                   |                           |      |    |
| Years                                  |                 |                                   |                           |      |    |
| < 5 years                              | 339 (24)        | 256 (25)                          | 83 (20)                   | **0.032** | 0.057 |
| ≥ 5 years                              | 1084 (76)       | 753 (75)                          | 331 (80)                  |       |    |
| Anthropometric data                    |                 |                                   |                           |      |    |
| Waist circumference (WC), cm           | 92.5 (14)       | 90.2 (12)                         | 100.0 (12)                | <0.001 | -  |
| WC ≥ 90 cm                             | 912 (63)        | 556 (54)                          | 356 (84)                  | <0.001 | 0.288 |
| Neck circumference (NC), cm            | 39.0 (4)        | 38.4 (3)                          | 40.3 (3)                  | <0.001 | -  |
| NC ≥ 40 cm                             | 558 (39)        | 296 (29)                          | 262 (63)                  | <0.001 | 0.316 |
| Chronic diseases                       |                 |                                   |                           |      |    |
| 1Hyperglycemia                         | 452 (32)        | 284 (28)                          | 168 (41)                  | <0.001 | 0.121 |
| 2Dyslipidemia                          | 1116 (78)       | 751 (74)                          | 365 (88)                  | <0.001 | 0.152 |
| 3Hypertension                          | 520 (37)        | 322 (32)                          | 198 (48)                  | <0.001 | 0.150 |
| Behavioral variables                   |                 |                                   |                           |      |    |
| 4Low physical activity                 | 693 (9)         | 485 (48)                          | 208 (50)                  | 0.311 | 0.050 |
| Smoking                                | 221 (16)        | 151 (15)                          | 70 (17)                   | 0.358 | 0.024 |
| 5Medium and high-risk nicotine         | 15 (1)          | 8 (1)                             | 7 (2)                     | 0.132 | 0.040 |
| Alcohol consumption                    | 886 (62)        | 621 (62)                          | 265 (64)                  | 0.384 | 0.023 |
| 6Medium and high-risk alcohol          | 147 (10)        | 99 (10)                           | 48 (12)                   | 0.316 | 0.027 |
| Seasonality                            |                 |                                   |                           |      |    |
| Winter                                 | 536 (37)        | 375 (37)                          | 165 (40)                  | <0.001 | 0.166 |
| Spring                                 | 525 (37)        | 360 (36)                          | 192 (46)                  |       |    |
| Autumn                                 | 148 (11)        | 135 (13)                          | 13 (3)                    |       |    |
| Summer                                 | 183 (13)        | 139 (14)                          | 44 (11)                   |       |    |
| Mining regions                         |                 |                                   |                           |      |    |
| Minas Gerais                           | 529 (36)        | 347 (33)                          | 182 (43)                  | <0.001 | 0.091 |
| Pará                                   | 932 (64)        | 692 (67)                          | 240 (57)                  |       |    |
| OSA risk assessment                    |                 |                                   |                           |      |    |
| Berlin questionnaire                   | 226 (16)        | 103 (10)                          | 123 (30)                  | <0.001 | 0.242 |
| NoSAS score                            | 475 (33)        | 224 (22)                          | 251 (61)                  | <0.001 | 0.370 |

OSA, obstructive sleep apnea; p-value of Pearson’s chi-square test; V, value of Cramer’s V test; WC, waist circumference; NC, neck circumference

Continuous variables are presented as median and interquartile ranges. Categorical variables are presented as absolute numbers and percentages. p-values in bold are the significant associations according to the chi-square test.

The data were compared using the chi-square analyses with Bonferroni correction. Cramer’s V was used as an effect size.

1Hyperglycemia, FPG ≥ 100 mg/dL or HbA1c ≥ 5.7%; 2dyslipidemia is classified when at least one of the parameters (TC, LDL, HDL, and TG) was altered or uses lipid-lowering drugs; 3hypertension, SBP > 140 mmHg or DBP > 90 mmHg; 4low physical activity (< 600 measure energy total—min/week); 5Fagerstrom test, medium- and high-risk nicotine consumption; 6AUDIT medium- and high-risk alcohol consumption
the young adults who were evaluated in our study. And also with the fact that the BQ may not be the most appropriate instrument for this population, since in category 2 questions are asked about excessive sleepiness when driving vehicles. Only 5% of workers were scored positively in this category, a value 79% lower than that found by Tan et al. (2017) in a study of the general population [46]. Demonstrating a possible high rate of BQ underreporting for our study sample, where the majority of shift workers, were heavy machine operators (e.g., off-road trucks capable of hauling 25–400 tons of mining material), and may have underreported this information due to their occupational role [45].

OSA is a multifactorial chronic disease, with risk factors well described in the literature, such as gender, age, obesity, alcohol, and tobacco consumption [7]. However, some recent studies have shown that vitamin D deficiency may be an important risk factor [21]. In our study, we found that, after adjusting for confounding variables, workers with vitamin D deficiency were 52 to 85% more likely to have a high risk for OSA by QB and NoSAS.

### Table 2 berlin questionnaire values (workers positive in each category) and NoSAS score criterion (workers positive in each criterion) of rotating shift workers according to vitamin D

| Categories of BQ, n (%) | Total (n = 1423) | Vitamin D | OR (95% CI) | p | V |
|-------------------------|------------------|-----------|-------------|----|----|
|                         | Normal (n = 1009) | Deficient (n = 414) |           |    |    |
| Category 1, positive    | 342 (24)         | 204 (20)  | 138 (33)    | 1.97 (1.52–2.54) | < 0.001 | 0.139 |
| Category 2, positive    | 68 (5)           | 43 (4)    | 25 (6)      | 1.44 (0.87–2.40) | 0.153    | 0.037 |
| Category 3, positive    | 666 (47)         | 360 (36)  | 306 (74)    | 5.11 (3.96–6.59) | < 0.001 | 0.348 |

**BQ**: Berlin questionnaire; **NC**: neck circumference; **OR**: odds ratio; **CI**: confidence interval; **p**: p-value of Pearson’s chi-square test; **V**: value of Cramer’s V test

The data were compared using the chi-square analyses with Bonferroni correction. Cramer’s V was used as an effect size. p-values in bold are the significant associations according to the chi-square test.

Category 1 of BQ includes five questions on snoring, category 2 three questions on daytime somnolence and sleepiness when driving, and category 3 one question on the history of hypertension and obesity. Overweight: BMI 25.0–29.9 kg/m²; obesity: BMI ≥ 30.0 kg/m²; Snoring: self-report of presence of snoring during sleep.

### Table 3 Odds ratio (95% confidence interval) of risk assessment of obstructive sleep apnea by vitamin D deficiency in rotating shift workers

| OSA risk assessment | Berlin questionnaire | NoSAS score |
|---------------------|----------------------|-------------|
| OR (95% CI)         | p        | AIC         | OR (95% CI) | p        | AIC         |
| Model crude         | 3.72 (2.77–4.98)    | < 0.001     | 5.40 (4.21–6.91) | < 0.001     | 1531.124   |
| Model adjusted 1    | 3.75 (2.77–5.06)    | < 0.001     | 5.19 (4.03–6.68) | < 0.001     | 1512.290   |
| Model adjusted 2    | 3.35 (2.44–4.59)    | < 0.001     | 4.36 (3.36–5.66) | < 0.001     | 1454.374   |
| Model adjusted 3    | 1.52 (1.06–2.18)    | 0.021       | 1.64 (1.09–2.48) | 0.018       | 1338.032   |

**OR**: odds ratio; **CI**: confidence interval

Multivariate logistic regression analysis to estimate the odds ratio of OSA risk in workers with vitamin D deficiency. Hosmer–Lemeshow test and Akaike information criterion (AIC) were used to assess the goodness-of-fit of the models. p-values in bold are the significant associations according to the logistic regression.

Model crude: prevalence of obstructive sleep apnea versus vitamin D deficiency
Model adjusted 1: model crude addition of seasonality, age, years of shift work, scholarly, skin color, and geographic location
Model adjusted 2: model adjusted 1 addition of hyperglycemia, dyslipidemia, and hypertension
Model adjusted 3: model adjusted 2 addition of body mass index, waist circumference, and neck circumference
score, respectively. Similar results were found by other studies, in which in patients with OSA, the higher the apnea-hypopnea index (AHI), the lower were the 25(OH)D levels [21]. However, caution is needed in interpreting the data, as there is an inverse association between vitamin D metabolites and excess body fat [9]. Goswami et al. (2016) discuss that the association between serum 25(OH)D (vitamin D) levels < 20 ng/mL and OSA may be explained by some confounding factors, mainly BMI and neck circumference [47]. In this regard, it is important to mention that workers with vitamin D deficiency were more likely to have witnessed snoring and apnea (BQ category 1). This finding is corroborated by other studies with objective measures of OSA, such as polysomnography [48]. Furthermore, when assessing NoSAS scores, we observed that workers with VDD were 59% more likely to self-report the presence of snoring during sleep, the main clinical predictor signal for OSA [43].

In addition to obesity, another extremely relevant risk factor for OSA occurrence is aging. Piovezan et al. (2017) verifying the association of vitamin D levels and apnea, found that individuals with 25(OH)D levels < 30 ng/mL had a higher percentage of OSA than individuals with 25(OH)D ≥ 30 ng/mL, only in participants over 50 years old [48]. This study demonstrated the association between vitamin D and OSA starting earlier (age ≥ 40 years) in shift workers. Also, in concordance with previous studies, the greater the chances of OSA with increasing age. Shift workers are at a higher risk of developing OSA because of the work schedule, which appears to contribute to the increased risk in younger adults. Vitamin D deficiency can lead to airway muscle hypertrophy and myopathy, consequently increasing the risk of developing obstructive sleep apnea [13]. In addition to OSA, aging also affects endogenous vitamin D synthesis. There is a decrease in concentrations of the precursor (7-dehydrocholesterol) of vitamin D in the skin with aging, decreasing its production from the sun’s rays [49].

Therefore, after adjusting for confounding variables, we concluded that workers with vitamin D deficiency are more likely to be at high risk for OSA, as measured by QB or NoSAS. We agree that the gold standard method for diagnosing OSA is polysomnography; however, it is an expensive test that requires qualified professionals and structure to be conducted. Thus, subjective analysis, through questionnaires or indicators, can provide very useful data for a better understanding of the presence of sleep apnea risk and its determinants.

The main limitations of this study are the variables obtained by self-report, which can lead to underestimation of risk behaviors or overestimation of protective behaviors. And also the lack of a group of regular daily workers to compare the results found in alternating shift workers. Additionally, the BQ use in shift workers may be a limitation of our study, due to the possibility that these workers could have fatigue and sleepiness due to the underlying shift work, and confound the findings. However, category 2 of BQ (which measures daytime sleepiness and fatigue) had the lowest percentage of positive scores (5%). To adjust for this, we also assessed the risk for OSA by the NoSAS score, which has no biases related to tiredness and sleepiness and has good predictive values for OSA [45, 50–52]. And finally, we included potential confounding variables to reduce measurement errors.

We consider as strengths of this study, the large sample of shift workers, as this is a difficult population to evaluate and is poorly studied. Furthermore, very little is explored in the literature about OSA in rotating shift workers, and also its relationship with deficient vitamin D levels. This is a population at risk for several comorbidities [29] and we encourage that similar studies be conducted with this population.
Rotating shift workers have a high risk for obstructive sleep apnea, and workers with vitamin D deficiency have higher chances of apnea, even after adjustment for confounding factors. However, only workers over 40 years with vitamin D deficiency were at increased risk for OSA. The impact of these comorbidities reinforces the need for prevention, early identification, and intervention on the potential health harms of these workers. More research should be conducted using direct methods, such as polysomnography examination to assess sleep in populations prone to OSA, as a way to promote healthy habits and prevent accidents.

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Declarations

Ethics approval All procedures involving human subjects were approved by the Research Ethics Committee of the Federal University of Ouro Preto (2012: CAAE: 0018.0.238.00-11; 2015 CAAE: 39682014.7.0000.5150; 2018: CAAE: 93760618.5.0000.5150).

Consent to participate This study was conducted according to the guidelines laid down in the Declaration of Helsinki and written informed consent was obtained from all subjects.

Consent for publication Informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors declare no competing interests.

References

1. Tufik S, Santos-Silva R, Tatdei JA, Bittencourt LRA (2010) Obstructive sleep apnea syndrome in the Sao Paulo Epidemiologic Sleep Study. Sleep Med 11:441–446.
2. Leng Y, McEvoy CT, Allen IE, Yaffe K (2017) Association of sleep-disordered breathing with cognitive function and risk of cognitive impairment: a systematic review and meta-analysis. JAMA Neurol. American Medical Association [cited 2022 Feb 22];74:1237–45. Available from: https://jamanetwork.com/journals/jama-neurol/fullarticle/2649259
3. Mehra R, Stone KL, Varosy PD, Hoffman AR, Marcus GM, Blackwell T, et al (2009) Nocturnal Arrhythmias across a spectrum of obstructive and central sleep-disordered breathing in older men: outcomes of sleep disorders in older men (MrOS sleep) study. Archives of internal medicine. Arch Intern Med [cited 2022 Feb 22];169:1147–55. Available from: https://pubmed.ncbi.nlm.nih.gov/19546416/
4. Heinz R, Vat S, Marques-Vidal P, Marti-Soler H, Andries D, Tobbback N et al (2015) Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study. Lancet Respir Med England 3:310–318
5. Benjafeld A V, Ayas NT, Eastwood PR, Heinz R, Ip MSM, Morrell MJ, et al (2019) Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. Lancet Respir Med 7
6. Mehra R, Principe-Rodriguez K, Kirchner HL, Strohl KP (2006) Sleep apnea in acute coronary syndrome: high prevalence but low impact on 6-month outcome. Sleep Med Netherlands 7:521–528
7. Senarathna C v., Perret JL, Lodge CJ, Lowe AJ, Campbell BE, Matheson MC, et al (2017) Prevalence of obstructive sleep apnea in the general population: a systematic review. Sleep Med Rev 34:70–81. Elsevier Ltd
8. Al Lawati NM, Patel SR, Ayas NT (2009) Epidemiology, risk factors, and consequences of obstructive sleep apnea and short sleep duration. Prog Cardiovasc Dis 51:285–293
9. Holick MF (2017) The vitamin D deficiency pandemic: approaches for diagnosis, treatment and prevention. Reviews in Endocrine and Metabolic Disorders. Rev Endocr Metab Disord 18;153–65
10. Berrisch SM, Sillau S, de Boer IH, Szklo M, Redline S (2015) 25-Hydroxyvitamin D concentration and sleep duration and continuity: multi-ethnic study of atherosclerosis. Sleep 38:1305–1311
11. Bozkurt NC, Cakal E, Sahin M, Ozkaya EC, Firat H, Delibasi T (2012) The relation of serum 25-hydroxyvitamin-D levels with severity of obstructive sleep apnea and glucose metabolism abnormalities. Endocrine. [cited 2019 Nov 3];41:518–25. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22246808
12. Massa J, Stone KL, Wei EK, Harrison SL, Barrett-Conner E, Lane NE, et al (2015) Vitamin D and actigraphic sleep outcomes in older community-dwelling men: the MrOS Sleep Study. Sleep. Oxford University Press (OUP); [cited 2020 Jul 16];38:251–7. Available from: https://academic.oup.com/sleep/article/38/2/251/2416956
13. McCarty DE, Chesson AL, Jain SK, Marino AA (2014) The link between vitamin D metabolism and sleep medicine. Sleep Med Rev. Elsevier Ltd; [cited 2020 Jun 29];18:311–9[https://doi.org/10.1016/j.smrv.2013.07.001
14. Liguori C, Romigi A, Igetti F, Mercuri NB, Cordella A, Tarquini E, et al (2015) Continuous positive airway pressure treatment increases serum vitamin D levels in male patients with obstructive sleep apnea. J Clin Sleep Med 11:603–7. American Academy of Sleep Medicine
15. Unnikrishnan D, Jun J, Polotsky V (2015) Inflammation in sleep apnea: an update. Reviews in endocrine & metabolic disorders. Rev Endocr Metab Disord; [cited 2020 Jul 16];18:153–65. Elsevier Ltd; [cited 2020 Jul 16];38:251–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22246808
16. Feldman D, Krishnan A, Moreno J, Swami S, Peehl DM, Srinivas S (2008) Vitamin D inhibition of the prostaglandin pathway as therapy for prostate cancer. Nutr Rev 65:S113–S115
17. Barceló A, de la Peña M, Barbé F, Pierola J, Bosch M, Agustí AGN (2007) Prostaglandin D synthase β trace) levels in sleep apnea patients with and without sleepiness. Sleep Med 8:509–511
18. Mete T, Yalcin Y, Berker D, Ciftci B, Guven SF, Topaloglu O et al (2013) Obstructive sleep apnea syndrome and its association with vitamin D deficiency. J Endocrinol Invest 36:681–685
19. Kerley CP, Hutchinson K, Bolger K, McGowan A, Faul J, Cormican L (2016) Serum Vitamin D is significantly inversely associated with
disease severity in Caucasian adults with obstructive sleep apnea syndrome. Sleep United States 39:293–300
20. Erdén ES, Genc S, Motor S, Ustun I, Ulutas KT, Bilgic HK et al (2014) Investigation of serum bisphenol A, vitamin D, and parathyroid hormone levels in patients with obstructive sleep apnea syndrome. Endocrine 45:311–318
21. Neighbors CLP, Noller MW, Song SA, Zaghi S, Neighbors J, Feldman D, et al (2018) Vitamin D and obstructive sleep apnea: a systematic review and meta-analysis. Sleep Med 43:100–8. Elsevier B.V.
22. Li X, He J, Yun J (2020) The association between serum vitamin D and obstructive sleep apnea: an updated meta-analysis. Respir Res 21:1. BioMed Central; [cited 2021 Aug 10]; 21:1–12. Available from: https://respiratory-research.biomedcentral.com/articles/10.1186/s12931-020-01554-2
23. Archontogeorgis K, Nena E, Papanas N, Steiropoulos P (2018) The role of vitamin D in obstructive sleep apnoea syndrome. Breathe. European Respiratory Society; [cited 2019 Oct 9]. p. 206–15. Available from: http://breathe.ersjournals.com/lookup/doi/10.1183/19840063.2018.01326.000618
24. McCarty DE, Reddy A, Keigley Q, Kim PY, Marino AA (2012) Vitamin D, race, and excessive daytime sleepiness. J Clin Sleep Med 8:693–697
25. Sowah D, Fan X, Dennett L, Hagtvedt R, Straube S (2017) Vitamin D levels and deficiency with different occupations: a systematic review. BMC Public Health. [cited 2018 Jun 18];17:519. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28637448
26. Sakamoto YS, Porto-Sousa F, Salles C (2018) Prevalence of obstructive sleep apnea in shift workers: a systematic review. Cien Saude Colet 23:3381–3392
27. Coppeta L, Papa F, Magrini A (2018) Are shiftwork and indoor work related to D3 Vitamin deficiency? A systematic review of current evidences. J Environ Publ Health
28. Branecky KL, Niswender KD, Pendergast JS (2015) Disruption of daily rhythms by high-fat diet is reversible. Cermakian N, editor. PLOS One 10:e0137970
29. Nascimento RA, Fajardo VC, Menezes-Júnior LAA de, Mendonça PHM, Nascimento MCVa, Tristão PMO et al (2021) Work hours as a risk factor for SARS-CoV-2 infections: cardiometabolic and sleep characteristics in rotating shift workers. Sleep Sci 15(Special 2):380. https://doi.org/10.5935/1984-0063.20210013
30. Babar T, Higgins-Biddle JC, Saunders JB, Monteiro MG (2001) The Alcohol use disorders identification test: guidelines for use in primary care. World Health Organization. Geneva, Geneva
31. Fagerström K-OO (1978) Measuring degree of physical dependence to tobacco smoking with reference to individualization of treatment. Addict Behav 3:235–41
32. IPAO RC (2005) Guideline for Data Processing and Analysis of the International Physical Activity Questionnaire (IPAQ): short and long forms 1–15
33. Prêcoma DB, de Oliveira GMM, Simão AF, Dutra OP, Coelho OR, Izar MC de O, et al (2019) Updated cardiovascular prevention guideline of the Brazilian society of cardiology – 2019. Arq Bras Cardiol 113:787–891
34. Friedewald WT, Levy RI, Fredrickson DS (1972) Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 18:499–502
35. Ada ADA (2018) Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2018. Diabetes Care 41:S13–27
36. Ferreira CES, Maeda SS, Batista MC, Lazaretti-Castro M, Vasconcelos LS, Madeira M, et al (2017) Consensus – reference ranges of vitamin D [25(OH)D] from the Brazilian medical societies. Brazilian Society of Clinical Pathology/Laboratory Medicine (SBPC/ML) and Brazilian Society of Endocrinology and Metabolism (SBEM). J Bras Patol Med Lab 53
37. Who WHO (2000) Obesity : preventing and managing the global epidemic : report of a WHO consultation. World Health Organization, Geneva
38. Ford ES (2005) Prevalence of the Metabolic Syndrome Defined by the International Diabetes Federation Among Adults in the U.S. Diabetes Care. Am Diab Assoc 28:2745–9
39. Martí-Soler H, Hirotsu C, Marques-Vidal P, Vollenweider P, Waebler G, Preisig M, et al (2016) The NoSAS score for screening of sleep-disordered breathing: a derivation and validation study. The Lancet Respiratory Medicine. Lancet Publishing Group; 4:742–8
40. Vaz AP, Drummond M, Caetano Mota P, Severo M, Almeida J, Carlos WJ (2011) Translation of Berlin questionnaire to Portuguese language and its application in OSA identification in a sleep disordered breathing clinic. Rev Port Pneumol Elsevier 17:59–65
41. Eloï M, Horváth DV, Szejnfeld VL, Ortega JC, Rocha DAC, Szejnfeld J et al (2016) Vitamin D deficiency and seasonal variation over the years in São Paulo, Brazil. Osteoporo Int Osteoporos Int 27:3449–3456
42. Young T, Evans L, Finn L, Palta M (1997) Estimation of the clinically diagnosed proportion of sleep apnea syndrome in middle-aged men and women. Sleep 20:705–706
43. Chaves Junior CM, Dal-Fabbro C, de Brun VMS, Tufik S, Bittencourt LIRA (2011) Brazilian consensus of snoring and sleep apnea – aspects of interest for orthodontists. Dent J Periodontal FapUNIFESP (SciELO) 16:e1–10
44. Abrishami A, Khajehdelhi A, Chung F (2010) A systematic review of screening questionnaires for obstructive sleep apnea. Can J Anesth 57:423–438
45. Menezes Júnior LAA, Fajardo VC, do Nascimento Neto RM, de Freitas SN, de Oliveira FLP, Pimenta FAP, et al (2021) Diagnostic accuracy of the Berlin questionnaire and the NoSAS score in detecting risk for obstructive sleep apnea in rotating shift workers. Sleep and Breathing. Springer International Publishing
46. Tan A, Yin JDC, Tan LWL, Van Dam RM, Cheung YY, Lee CH (2017) Using the Berlin questionnaire to predict obstructive sleep apnea in the general population. J Clin Sleep Med 13:427–32. American Academy of Sleep Medicine
47. Goswami U, Ensrud KE, Paudel ML, Redline S, Schernhammer ES, Shikany JM, et al (2016) Vitamin D concentrations and obstructive sleep apnea in a multicenter cohort of older males. Ann Am Thorac Soc. American Thoracic Society; 13:712–8.
48. Piovezan RD, Hirotsu C, Feres MC, Cintra FD, Andersen ML, Tufik S et al (2017) Obstructive sleep apnea and objective short sleep duration are independently associated with the risk of serum vitamin D deficiency. PLOS ONE 12:1–11
49. MacLaughlin J, Holick MF. Invest J(1985) Aging decreases the capacity of human skin to produce vitamin D3. Find the latest version. Am J Clin Nutr 76:1536–1538
50. Herschmann S, Berger M, Habra-Rubio J, Heinzer R (2021) Comparison of NoSAS score with Berlin and STOP-BANG scores for sleep apnea detection in a clinical sample. Sleep Med 79:113–116
51. Giampá SQC, Pedrosa RP, Gonzaga CC, Bertolami A, Amodeo C, FapUNIFESP (SciELO) 16:e1-10
52. Coutinho Costa J, Rebelo-Marques A, Machado JN, Gama JMR, Piovezan RD, Hirotsu C, Freitas SN, de Oliveira FLP, Feres MC, Schernhammer ES, Shiikany JM et al (2016) Vitamin D concentrations and obstructive sleep apnea in the general population. J Clin Sleep Med 12:427–32. American Academy of Sleep Medicine