ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 8, Issue – 3, June – 2023 , Page No. : 213 – 219

Association of obstructive sleep apnoea with vitamin D deficiency in Bikaner

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Citation this Article: Mohd. Zeeshan, B. K. Binawara, D. K. Devra, Nishanta, "Association of obstructive sleep apnoea with vitamin D deficiency in Bikaner", IJMSIR- June - 2023, Vol – 8, Issue - 3, P. No. 213 – 219.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Introduction: Obstructive Sleep Apnoea (OSA) is the commonest sleep associated breathing disease, chara cterized by recurrent episodes of upper airway occlusion (partial or complete) leading to recurrent arterial hypo xaemia and sleep fragmentation. It is common, with a prevalence of 10–17% among men and 3–9% among women. Vitamin D causes inhibition of the secretion of pro-inflammatory T-helper cell Th1 cytokines and favours the production of anti-inflammatory Th2 cyto kines. Thus, deficiency of vitamin D causes inflammation of muscles of airway, which further causes OSA.

Aims and Objectives: To analyse and compare the general physical examination, oxygen saturation and serum vitamin D level of patients of Obstructive Sleep Apnoea and healthy control.

Materials and Methods: A case control study was conducted in Departments of Physiology and Medicine, S. P. Medical College, Bikaner. A total No. of 50 cases and 50 controls were selected for the study. In both groups, general physical examination was done, oxygen saturation and serum vitamin D level were analysed and compared.

Results: Mean vitamin D level was 21.87 ng/ml. with SD of 2.21 in control group, whereas mean vitamin D level was 16.69 ng/ml. with SD of 1.20 ng/ml. in case group. In control group, no subject belonged to deficient (< 20 ng/ml.) group, 48 (96%) subjects in insufficient (20-29 ng/ml.) and 2 (4%) subjects in optimal (>30 ng/ml.) group were there. In case group, 50 (100%) were belonged to deficient (< 20 ng/ml.) group and no subject was there in insufficient (20-29 ng/ml.) and optimal (>30 ng/ml.) group.

Conclusion: The association between vitamin D defici ency and OSAS is mediated by complex patho genetic mechanisms. Vitamin D deficiency appears to be common among OSAS patients. Further research is need ed to fully elucidate the relationship and the mechanisms of vitamin D insufficiency in OSAS and any need for supplementation.

Keywords: Obstructive Sleep Apnoea, Obstructive Sleep Apnoea Syndrome, Vitamin D deficiency

Introduction

Obstructive Sleep Apnoea (OSA) is the commonest sleep associated breathing disease. It is a major health issue with multiple comorbidities. Obstructive Sleep Apnoea syndrome (OSAS) is characterized by recurrent episodes of upper airway occlusion (partial or complete) leading to recurrent arterial hypoxaemia and sleep fragmentation [1]. There are recurrent events of reduction of airflow or cessation of airflow due to partial or complete collapse of upper airway during sleep. These events are known as "hypo pnoea" in case of partial cessation of breathing, or apnoea" in case of complete obstruction of airway. In both cases, reduction in oxygen saturation (SpO_2), distur bance in sleep, or both may occur. High recurrence of apnoea or hypo pnoea during sleep may result into disturbance in sleep in combination with decreased SpO_2. This leads to negative effect to quality of life and health status. The Obstructive Sleep Apnoea syndrome (OSAS) or obstructive sleep apnoea–hypo pnoea syndrome (OSA HS) is referred to OSA associated with daytime symptom i.e., increased sleepiness during daytime, reduced cogni tive functions etc.

Nowadays, it is common, with a prevalence of 10–17% among men and 3–9% among women in the developed world [2]. The pathogenesis of OSAS remains unclear and is probably multifactorial, including various mechan isms such as inflammation and oxidative stress [3]. Obesity is the most important risk factor and is report ed in up to 70% of cases. Additional risk factors include older age, male sex, ethnicity and family history [4]. Of interest, OSAS seems to exhibit a seasonal predominance pattern with higher incidence and severity occurring in winter [5]. Vitamin D is the fat-soluble vitamin existing in two forms: ergocalciferol or vitamin D2, obtained through dietary sources; and cholecalciferol or vitamin D3, produced in the skin after exposure to sunlight [6]. Serum 25-hydroxyvitamin D (abbreviated: 25(OH)D) is considered the best indicator of vitamin D status. The most important function of vitamin D is regulation of bone homeostasis [7].

Vitamin D is also implicated in several non-skeletal conditions, including cardiovascular disease, cancer, auto immune disorders and diabetes mellitus [8]. The OSAS and vitamin D deficiency share the same risk factors and comorbidities, particularly older age, obesity, renal failure and diabetes, while both conditions present comm on pathogenic features (e.g., inflammation) [9].

Deficiency of vitamin D is related to increased auto immunity and sensitivity to infection. Anti-microbial effects of monocytes and macrophages are enhanced by Calcitriol, which employs an important role in infections such as tuberculosis. Low level of serum 25(OH)D is related to increased incidence of chronic obstructive pulmonary disease (COPD), upper respiratory tract infections (URTI), allergic asthma and allergic rhinitis. Repeated infections and disruption in immune system may encourage the development of hypertrophy of tonsils and chronic rhinitis. Both of these conditions are also risk factors for of OSA. In addition, vitamin D also causes inhibition of the secretion of pro-inflammatory T-helper cell Th1 cytokines e.g., IL-2, interferon-γ and TNF-α and favours the production of anti-inflammatory Th2 cyto kines e.g., IL-3, IL-4, IL-5 and IL-10. Thus, defici ency of vitamin D causes inflammation of muscles of air way, which further causes OSA.

Aims and Objectives: To analyse and compare the general physical examination, oxygen saturation and serum vitamin D level of patients of Obstructive Sleep Apnoea and healthy control.

Materials and Methods

- Study design: Case Control study

- Study place: Department of Physiology with Depart ment of Medicine, S. P. Medical College and Associated group of P.B.M. Hospitals, Bikaner
- Sample size: 50 cases and 50 controls
- Sampling method: Simple Random sampling

Inclusion criteria

- Patients suffering from Obstructive Sleep Apnoea
- Age between 18 to 70 years

Exclusion criteria

- Patients not willing to participate
- Smoker
- Alcoholic
- Age less than 18 years
- Patients suffering from chronic illness
- Patients on medication i.e. Beta blockers, SSRIs, Amphetamines, Caffeine, Theophylline etc.
- Patients suffering from insufficient sleep, de pression, narcolepsy, hypo thyroidism, restless leg syndrome, dystrophic a myotonic a etc.

Data Collection

A total number of 50 cases of Obstructive Sleep Apnoea and 50 healthy controls from general population were selected for the study. Complete medical history was taken with special focus on breathing symptoms, sleep disorders. General physical examination including assessment of height, weight, Body Mass Index (BMI), waist circumference, blood pressure and oxygen sat uration was done. For evaluation of haemato-biochemical parameters 10 ml. of blood was collected from each of the subjects. Different parameters viz. Haemoglobin (HB), Total Leucocytes Count (TLC), Differential Leuco cytes Count (DLC) viz. neutrophils, eosinophils, baso phils, lymphocytes and monocytes, Total Platelet Count, Erythrocyte Sedimentation Rate (ESR) and Packed Cell Volume (PCV) were evaluated. Serum level of Vitamin D was estimated. All these haemato-biochemical estimate ons were done following laid down standard procedures.

Data Analysis

Statistical analysis of collected data was done. Mean values for different data collected in the appropriate groups and differences between means by 't' test and 'chi' square test were calculated. The data analysis was done using SPSS for Windows version 21 (SPSS Inc, IL). Results were prepared as mean ± SD in tables.

Observations and Results

Table 1: distribution of control group and case group subjects according to age, sex and Bmi

Parameter	Control Group		Case Group		Chi square test	p value	t value
	No	%	No.	%			
Age groups (In Years)					13.593	0.004	-
≤ 35	23	46	11	22			
36-50	13	26	30	60			
51-65	14	28	8	16			
> 65	0	0	1	2			
Mean	39.04		41.58				
SD	14.70		12.33				
Gender					12.965	0.0001	-
Female	15	30	34	68			
Male	35	70	16	32			
BMI ($Kg/m.^2$)					-	0.0001	62.830
<18.5	0	0	0	0			
18.5-24.9	37	74	0	0			
25-29.9	8	16	45	90			
≥30	5	10	5	10			

The distribution of control group and case group subjects according to age has been summarized in Table –1. The mean age for case group was 41.58 years and for control group it was 39.04 years. In case group, majority of the subjects belonged to 36-50 years of age group with 30 (60%) subjects. In control group, majority of the subjects belonged to ≤ 35 years of age group with 23 (46%) subjects.

The sex distribution in control group and case group subjects has been summarized in Table – 1. In case group, out of 50 subjects, 34 (68%) were female and 16 (32%) were male. In control group, out of 50 subjects, 15 (30%) were female and 35 (70%) were male.

The BMI status of control group and case group subjects has been summarized in Table – 1. In control group, no subject was there in ≤ 18.5 BMI range, 37 (74%) subjects were in 18.5-24.9 BMI range, 8 (16%) subjects belonged to 25-29.9 BMI range and 5 (10%) were belonged to ≥ 30 BMI range. In case group, no subject was there in ≤ 18.5 and 18.5-24.9 BMI range, 45 (90%) were in 25-29.9 BMI range and 5 (10%) were belonged to ≥ 30 BMI range.

Table 2: vitamin d status of control group and case group subjects

Parameter	Control Group		Case Group		Chi square test	p value	t value
	No.	%	No.	%			
Vitamin d status							
Deficient (<20 ng/ml)	0	0	50	100	100	0.0001	-
Insufficient (20-29 ng/ml)	48	96	0	0			
Optimal (≥30 ng/ml)	2	4	0	0			
Vitamin D Level (ng/ml.)					-	0.0001	14.565
Mean	21.87		16.69				
SD	2.21		1.20				

The Vit. D status of control group and case group subjects has been summarized in Table – 2. Out of 50 control subjects, no subject belonged to deficient (< 20 ng//ml.) group, 48 (96%) subjects in insufficient (20-29 ng/ml.) and 2 (4%) subjects in optimal (>30 ng/ml.) group were there. Out of 50 case subjects, all the 50 (100%) were belonged to deficient (< 20 ng//ml.) group and no subject was there in insufficient (20-29 ng/ml.) and optimal (>30 ng/ml.) group.

The mean and SD values of vitamin D in control group and case group subjects have been summarized in Table – 2. Mean vitamin D level was 21.87 ng/ml. with SD of 2.21 ng/ml. in control group and 16.69 ng/ml. with SD of 1.20 ng/ml. in case group.

Discussion

The available literature emphasizes the association between OSAS and a number of disorders, such as cardiovascular disease, impaired glucose metabolism and other endocrinopathies, such as hypercortisolism and osteoporosis.

There is a definitive anatomic and epidemiological association between abnormalities in sleep and vitamin D deficiency. It is supported by the presence of vitamin D receptors in the anterior and posterior hypothalamus, substantia nigra, midbrain central gray, raphe nuclei, and the basal forebrain, the same areas which are considered to play a role in the initiation and maintenance of sleep. The hypothalamus, its associated projections, and the nucleus reticularis pontis appear to coordinate the sleep / wake state and the paralysis of the bulbar and somatic musculature during sleep. Pacemaker cells of the brainstem appear to play an important role in the timing of sleep. Effects of Vit. D on these brain areas may provide an explanation for seasonal variations in sleep seen in normal humans, as well as suggesting a treatable aetiology for the current epidemic of sleep disorders.

Many conditions interfere with the endogenous synthesis of vitamin D such as low sun exposure, race / ethnicity and skin color, season, altitude, and latitude.

Demographic data

In the present study 30 (60%) subjects belonged to 36-50 years of age group. In control group, 23 (46%) subjects belonged to ≤ 35 years of age group. The mean age for

case group was 41.58 years and for control group it was 39.04 years as mentioned in table - 1.

In case group, out of 50 subjects, 34 (68%) were female and 16 (32%) were male. In control group, out of 50 subjects, 15 (30%) were female and 35 (70%) were male as mentioned in table - 2.

Mete T et al [6] have reported the mean age for case group as 47.21years and for control group it as 46.9 years. There were 75 females and 75 males present in case group while 16 females were seen in control group. Demographic features of all OSAS and control groups were similar between two groups and no significant difference could be detected ($p>0.05$).

A study by Devika *et al* [7] revealed that more males (53.3 %) had complaints of excessive daytime sleepiness as compared to females. The average age of present study population was 36 + 14.6 years.

Yang SQ et al [8] found that the average age was 57.4±12.7 years (range 16–90 years). The average ages of subjects with and without OSA were 57.7±12.4 years (range 16–88 years) and 55.2±14.1 years (range 25–90 years), respectively.

Jennum P et al [9] have reported that OSAS prevalence was increased at the age of 18-45 and form a plateau between the ages 55-65 years.

BMI analysis

In the present study it was found that in case group, no subject was there in ≤ 18.5 and 18.5-24.9 BMI range, 45 (90%) were in 25-29.9 BMI range and 5 (10%) were belonged to ≥ 30 BMI range. In control group, no subject was there in ≤ 18.5 BMI range, 37 (74%) subjects were in 18.5-24.9 BMI range, 8 (16%) subjects belonged to 25-29.9 BMI range and 5 (10%) were belonged to ≥ 30 BMI range.

Study by Bonnet L et al [10] revealed that both overweight OSA patients and obese OSA patients had low levels of vitamin D, indicating that BMI and OSA interact to influence the vitamin D level. A high BMI and OSA are causally interrelated.

One study confirmed that low circulating levels of vitamin D were associated with obesity in humans, and obesity was thought to be one of the reasons for the reduction in the 25(OH)D level. According to the source, metabolism and various influencing factors of vitamin D.

Fan et al [11] reported that vitamin D was negatively correlated with BMI and that there was an interaction between the vitamin D level and obesity. Mete T et al [25] found that mean BMI for OSAS group was 32.8 kg/m2 and for control group it was 32.02 kg/m^2.

Vitamin d deficiency and sleep apnoea

In present study out of 50 case subjects, 50 (100%) were belonged to deficient (< 20 ng//ml.) group and no subject was there in insufficient (20-29 ng/ml.) and optimal (>30 ng/ml.) group. Out of 50 control subjects, no subject belonged to deficient (< 20 ng//ml.) group, 48 (96%) subjects in insufficient (20-29 ng/ml.) and 2 (4%) subjects in optimal (>30 ng/ml.) group were there. The Mean vitamin D level was 16.69 ng/ml. with SD of 1.20 ng/ml. in case group, whereas mean vitamin D level was 21.87 ng/ml. with SD of 2.21 in control group. Result was found significant with 0.0001 p value. Results were corelated with t value 14.565.

Devika et al [7] found that a prominent number (96 %) of subjects suffering from excessive day time sleepiness showed an insufficiency of vitamin D. Of these a majority (53.3 %) had vitamin D values between 11 ng / dl to 20 ng / dl, with a mean value of 16.6 + 9.1.

Mete T et al [6] found that no significant difference could be detected between OSAS and the control groups for 25(OH)D levels ($p>0.05$). Evaluation of serum 25(OH)D levels of OSAS subgroups revealed a significantly lower level in severe OSAS group than in the other three

groups. No significant difference was detected at percentage of subjects with a serum 25(OH)D level below 20 µg/dl between control group and mild and moderate OSAS groups, and between mild and moderate OSAS groups (p=0.654, p=0.822, p=0.424; respectively). In a similar study by Bozkurt NC et al [12], the relationship between OSAS, glucose metabolism, and 25(OH)D level was examined, and OSAS patients were shown to have lower rate of 25(OH)D as well as higher insulin resistance, prediabetes, and diabetes than controls. Kerley et al [13] found that vitamin D was inversely associated with OSA severity. They concluded that vitamin D deficiency is strongly linked to OSA more than vitamin D insufficiency.

Conclusion

Sleep disorders have now become a relevant socioeconomic problem beyond a simple public health issue. It thus becomes important to find and promote adequate solution for reducing its impact on health resources and health economy. Vitamin D could play a promising role in sleep disorders. The association between vitamin D deficiency and OSAS is mediated by complex pathogenetic mechanisms and affected by multiple confounding factors. The fact that vitamin D deficiency appears to be common among OSAS patients suggests that screening should be performed when clinically indicated. The positive effects of vitamin D in the comorbidities associated with OSAS (e.g. cardiovascular disease) need to be considered, especially in the context of the relatively limited cost of vitamin D supplementation. Further research with appropriate adjustments for potential confounders is needed to fully elucidate the relationship and the mechanisms of vitamin D insufficiency in OSAS and any need for supplementation.

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