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Original Article

Effect of Obstructive Sleep Apnea on Bone Mineral Density

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Abstract

OBJECTIVE: Various studies have suggested that obstructive sleep apnea (OSA) affects bone metabolism. One of the most significant factors is hypoxia which induces certain transcription factors that stimulate bone osteoclastic activity. It also induces respiratory acidosis and oxidative stress which enhances bone resorption. Leptin and melatonin secretions are regulated by the circadian system which is affected due to sleep fragmentation in OSA. Other comorbidities associated with OSA such as vitamin D deficiency, hypogonadism, obesity, and insulin resistance are indirect mechanisms that affect bone mineral density (BMD).

MATERIAL AND METHODS: This is a prospective case–control study. All patients having symptoms of sleep-related breathing disorder (excluding post-menopausal females or patients with known case of osteoporosis or any other clinical illness which is a direct cause of osteoporosis) attending the Sleep Out Patient Department (OPD) were screened for OSA as per the STOPBANG questionnaire scoring system. Participants having score >2 constituted the final study population and were subjected to the polysomnography test. Participants with an apnea-hypopnea index (AHI) > 5 in polysomnography were considered as cases and those with AHI <5 were considered as controls. Both the groups were then subjected for dual-energy X-ray absorptiometry (DEXA) scan and vitamin D to establish a comparison.

RESULTS: Out of 93 participants, 59 were taken as cases (OSA group), whose mean age was 48.02 (±8.435) years, mean body mass index (BMI) was 33.73 (±7.48) kg/m^2, mean neck circumference was 37.8 cm (±5.08) as compared with the age, sex, and BMI matched non-OSA control group (n = 34). Mean BMD in the case group was found to be significantly on the lower side as compared with the control group (−2.02 ± 1.09 vs. −1.03 ± 0.97) (P < .001) when compared in Z score, while (0.885 ± 0.535 vs. 0.933 ± 0.616) when compared in g/cm^2 (P < .001), with negative correlation between AHI and BMD (r = −0.507, P < .001). Mean vitamin D level in the case group was at a lower level as compared to the control group (21.02 ± 7.27 vs. 24.48 ± 6.92, P < .05), with negative correlation between AHI and serum vitamin D level (P < .001, r = −0.286).

CONCLUSION: OSA affects BMD by various pathophysiologic mechanisms. The AHI is inversely correlated with BMD; that is, with increasing severity of OSA, there is a decrease in BMD.

KEYWORDS: Obstructive sleep apnea, Bone mineral density
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INTRODUCTION

Sleep-disordered breathing (SDB) is a common medical disorder associated with various common comorbidities.[1] Recognition of its relevance in medicine is relatively recent. Obstructive sleep apnea (OSA) along with central sleep apnea, periodic breathing, and sleep-related hypoventilation collectively come under sleep breathing disorders. OSA is considered more prevalent.

OSA is characterized by recurrent episodes of partial or complete upper airway collapse during sleep. The collapse is highlighted by a reduction in, or complete cessation of, airflow despite ongoing inspiratory efforts. Respiratory disturbances during sleep dramatically interfere with brain and other organ functions such as cardiovascular, neurologic, endocrine, and mental disorders as well as the skeletal system, especially bone.[2] Various mechanisms have been proposed, which proves that OSA effects bone mineralization. When sleep apnea periodically deprives the body of oxygen, it can weaken bones and raise the risk of osteoporosis.[3,4] Hypoxia induces certain transcription factors which in turn stimulates osteoclastic activity and inhibits osteoblastic activity.[5,6] It also induces respiratory acidosis due to hypercapnia and oxidative stress which enhances bone resorption. Leptin and melatonin are powerful inhibitors of bone mass accrual, and as their secretion is regulated by the circadian system which is disturbed due to sleep fragmentation in OSA, it also becomes one of the important factors affecting bone mineralization.[7-9] Inflammatory markers including IL-1β, IL-6, and TNF-α are elevated in OSA and in obesity,[10] and these markers are known regulators of the RANK/RANKL/OPG system and induce osteoclast differentiation and/or activation.[3] OSA-associated comorbidities such as vitamin D deficiency leading to secondary hyperparathyroidism, hypogonadism, insulin resistance, and obesity are other indirect mechanisms affecting bone mineral density (BMD).[11,12] In addition, OSA has been associated with impaired cognitive function, memory, and motor function which contribute to increased risk of falls and accidents and, hence, increased risk of fracture.[13]

Aim of the Study

Primary Objective: To study the effect of OSA on BMD

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Secondary Objective: To study the effect of OSA on serum vitamin D level

MATERIAL AND METHODS

Study Design
Case–control prospective study.

Study Area
Department of Respiratory Medicine in collaboration with Centre of Diabetes, Department of Endocrinology, Aligarh, after getting approval from the Institutional Ethical Committee.

Duration of Study
Eighteen months from December 2017 to September 2019 (this includes duration of participation of subjects only).

Study Population
People attending the Respiratory Medicine Out Patient Department (OPD) in Medical College and Hospital between ages 30 and 60 years complaining of sleep-related problems were considered for this study. People with age < 30 years hardly complained of any sleep-related breathing disorder, and most of the people with age > 60 years had already developed age-related osteoporotic changes. Hence, both the age groups were excluded from the study.

Sample Technique
The study population was first screened for SDB using the STOPBANG questionnaire. Those having STOPBANG score > 2 were further taken for the study. Exclusion criteria as mentioned below were applied to the screened population and were filtered out from the study. The remaining participants were subjected to polysomnography which was done in a level I sleep lab using 32 leads with the ALICE 6 LDe system. Participants with AHI > 5 in polysomnography were taken as cases. While age, sex, and BMI matched participants of the same screened population with AHI < 5 were taken as controls.

The following data were compiled in all participants:

- Written informed consent was taken and recorded in the predesigned performa,
- Clinical history and demographic data was recorded in the predesigned performa,
- Weight, height, BMI (weight in kg/ht in m^2), neck circumference, blood pressure, serum glucose, total cholesterol, triglyceride, thyroid profile, parathormone (PTH), and serum calcium were recorded to rule out other causes of decreased BMD.

MAIN POINTS

- This study showed the effect of OSA on BMD; with increasing severity of OSA there was a decrease in BMD.
- This study revealed an inverse relation between severity of OSA and Vitamin D levels.
- This study suggest that there is a positive correlation between severity of obesity and OSA.

Inclusion Criteria
- All OPD based patients aged 30-60 years having a sleep-related disorder and giving consent to undergo sleep study were included in the study.

Exclusion Criteria
- Age < 30 years or > 60 years,
- Post-menopausal women both natural and surgical,
- Known case of osteoporosis,
- Critically ill patients,
- Cushing syndrome,
- Hyper/hypothyroidism,
- Hyper-parathyroidism,
- Vitamin D deficiency,
- Diabetes mellitus,
- Bone malignancy,
- Rheumatoid arthritis,
- Chronic liver disease or chronic renal disease,
- Prolong use of steroids, and
- All patients who are already diagnosed with other medical conditions which are directly a cause of decreased BMD.

Investigations

Sleep Study
All participants underwent nocturnal sleep assessment in a level I sleep lab using 32 leads with PHILIPS ALICE 6 Lade system. The following parameters were measured: snoring sound, electrocardiogram, pulse transit time, airflow, nasal pressure, respiratory efforts, body position, and oxygen saturation (SaO_2) by pulse oximeter. Hypopnoea was defined as a 30% or greater reduction in airflow from the baseline value lasting for at least 10 seconds or associated with at least ≥ 4% oxygen desaturation from the base line.[14] Apnea was defined as the absence of airflow on the nasal cannula lasting for > 10 seconds.[14] The absence of rib cage movements associated with apnea defined the event as central, whereas a progressive increase in pulse transit time and respiratory efforts event was defined as obstructive apnea. The apnea-hypopnea index (AHI) was defined as the ratio of the number of episodes of apnea or hypopnea per hour of reported sleep time. Maximum and minimum SaO_2 was recorded during sleep. OSA was diagnosed as per the diagnostic criteria of the American Academy of Sleep Medicine.[15] An AHI > 5 and < 15 indicated mild OSA, AHI ≥ 15 and < 30 indicated moderate OSA, and an AHI ≥ 30 denoted severe OSA.[15]

DEXA Scan
Bone metabolism was measured using a whole-body dual-energy X-ray absorptiometry (DEXA) scanner (Hologoic QDR-4500). The standard procedures described by Salmona et al. in the literature for DEXA measurement were applied.[16] BMD was measured in all patients at the neck of the femur and at the lumbar spine (L1-L4). BMD was expressed in g/cm^2 and as standard deviations (SD) from the normal average value of peak bone mass (T score). According to their BMD results for the femoral neck and lumbar spine, participants were classified into 3 groups according to World Health Organization criteria:

- Normal BMD (T score > −1.0 SD),
- Osteopenia (T score −1.0- −2.5 SD), and
- Osteoporosis (T score < −2.5 SD).

Serum Vitamin D

Five milliliters of arterial blood sample were drawn from all consenting participants (both case and controls) who underwent sleep study overnight. Samples were collected in plain vials and then sent to Rajiv Gandhi Centre of Diabetes, JNMCH, at room temperature for vitamin D level analysis. This was done using Beckman Coulter Access 2 machine working on the principle of chemiluminescence immunoassay (CLIA). The normal reference range for vitamin D level was taken from 25 to 80 ng/dL.

Statistical Analysis

This was a hospital-based case–control cross-sectional study. Data was analyzed by using the Statistical Package for Social Sciences version 25.0 software (IBM Corp.; Armonk, NY, USA). All numerical (scale) variables such as BMD, BMI, and serum vitamin D were presented as mean ± SD with 95% confidence interval while frequency of distribution was used for non-numeric variables. Attempts were made to represent data graphically as far as possible. The mean of variables between the different groups were compared using ANOVA and Student's *t*-test. Frequencies of distribution were calculated using the chi-square statistical method. All reported *P* values are 2-tailed, and a *P* value of < .05 was considered significant. The Pearson correlation coefficient was calculated between AHI and BMD and between AHI and vitamin D to establish an association.

OBSERVATION AND RESULTS

Flow Chart of the Study

Distribution of Study Population: A total of 93 participants were subjected to polysomnography (Table 1), out of which 59 (63.4%) had AHI > 5 (taken as cases), while 34 (36.6%) had AHI < 5 (taken as controls). In the study, 15 participants (16.1%) had mild OSA, 17 (18.3%) had moderate OSA, and 27 (29%) had severe OSA. Maximum participants were of the age group between 41 and 50 years (37 in number (39.8%)) followed by 31 participants (33.3%) in the 51-60 age group, and then 25 participants (26.9%) in the 31-40 age group. Age distribution of the study population is depicted in Figure 1.

Relation Between AHI and Age

Most of the moderate to severe OSA cases lay between 51 and 60 years of age. With increasing age, prevalence of OSA as well as severity of OSA also increases. Prevalence of OSA in different age groups in this study is depicted in Figure 2. Mean AHI was maximum in the 51-60 years age group (48.72 (± 29.63)), followed by the 41-50 years group (45.46 ± (32.35)), and minimum in the 31-40 years group (31.08 ± (26.5)). The same is depicted in Figure 3. On comparing mean AHI in the different age groups using ANOVA test (*F* value 8.62 and *P* < .05), it was concluded that with increasing age there is an increase in AHI.

Table 1. Overall Profile (in Mean SD) of the Study Population

Profile	Case (n = 59)	Control (n = 34)
Age (years)	47.97 ± 8.42	46.35 ± 7.29
Sex		
M	50	28
F	9	6
Weight (kg)	86.9 ± 18.14	78.81 ± 16.94
Height (cm)	159.63 ± 19.6	162.62 ± 13.56
BMI (kg/m^2)	33.73 ± 7.48	29.66 ± 4.88
Neck circumference (cm)	37.87 ± 5.08	29.53 ± 2.6
Mean AHI	43.13 ± 30.21	4.43 ± 0.65
BMD at femoral neck (T score)	−1.98 ± 1.16	−1.03 ± 0.955
BMD at lumbar spine (T score)	−1.97 ± 1.15	−0.98 ± 0.96
Mean BMD (T score)	−2.02 ± 1.09	−1.03 ± 0.97
Mean BMD (g/cm^2)	0.86 ± 0.053	0.933 ± 0.61
Vitamin D (ng/dL)	21.02 ± 7.27	24.48 ± 6.9

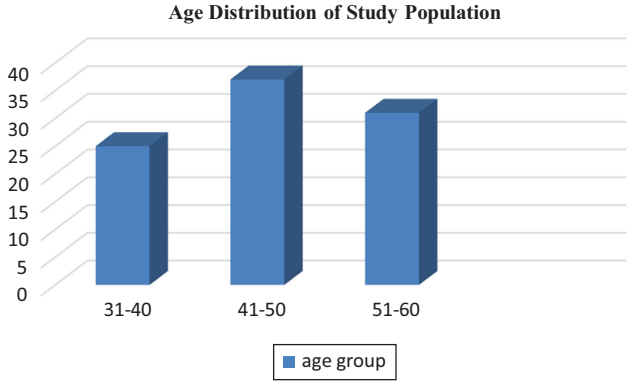

Figure 1. Age distribution of the study population.

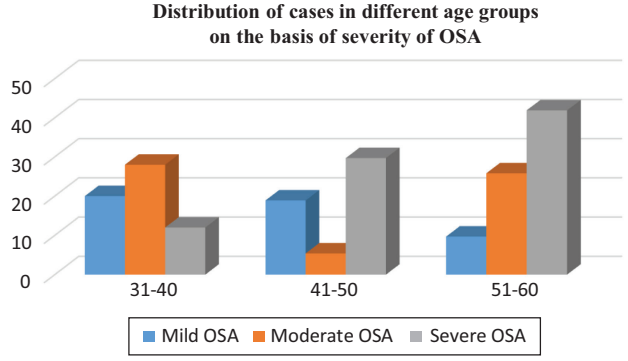

Figure 2. Distribution of cases in the different age groups on the basis of severity of OSA.

Relation Between OSA and Gender

Mean AHI in the overall case group was 43.13 ± (30.21). Mean AHI in males was 43.76 ± (30.92) with a minimum

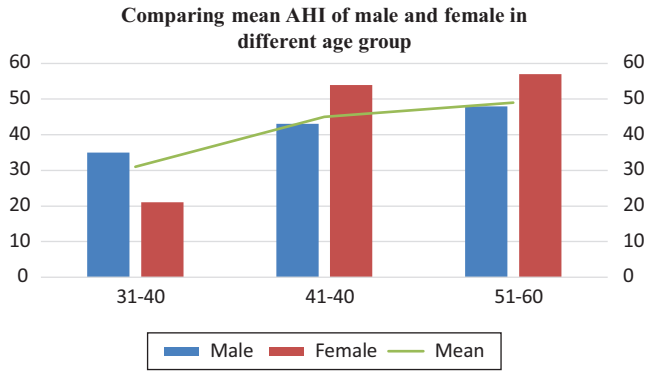

Figure 3. Comparison of mean AHI of males and females in the different age groups.

value of 7 and a maximum value of 115, while in females it was 39.6 ± (27.30) with a minimum value of 14 and a maximum value of 85.5 (Figure 3). The severity of OSA is independent of sex when compared within the same age group using Student's *t*-test (*P* value > .707).

Distribution of the Study Population as per the WHO Classification of Obesity

Out of the 59 cases, 16 (27.1%) participants lay in the obesity class I group followed by 15 (25.4%) participants in the class III group followed by 13 (22%) in the overweight class, followed by 8 (13.6%) in the obesity class II group, and then 7 (11.9) in the normal weight group. This distribution is depicted as a pie chart in Figure 4.

The maximum number of severe OSA cases lay in the obesity class III group (10), followed by the obesity class II group (6), the class I group (5), and the overweight (3) and normal weight (3) groups (Figure 5). Statistically significant data suggests that with increasing severity of obesity, the frequency of severe OSA increases. Hence, OSA is more prevalent in the obese population (Fisher's exact test, $F = 24.118$, $P < .05$).

Correlation Between AHI and Body Mass Index (BMI)

A positive correlation was established between BMI and AHI using Pearson's correlation test ($r = 0.434$, $P < .05$) as depicted in Figure 6.

Corelation Between OSA and BMD

On comparing mean BMD (mean BMD at LS spine and femoral neck) in the different severity classes of OSA, it was found that there is a decrease (more negative value) in mean BMD with increasing severity of OSA. Mean BMD in mild OSA was −1.26(± 0.69), moderate OSA was −1.73 ± (1.14), whereas in severe OSA it was −2.62 ± (0.90). The result was statistically significant using ANOVA test ($F = 15.03$, $P < .001$) (Figure 7).

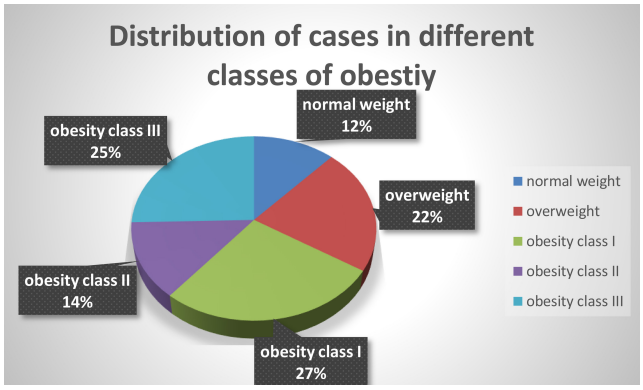

Figure 4. Distribution of cases according to severity of OSA.

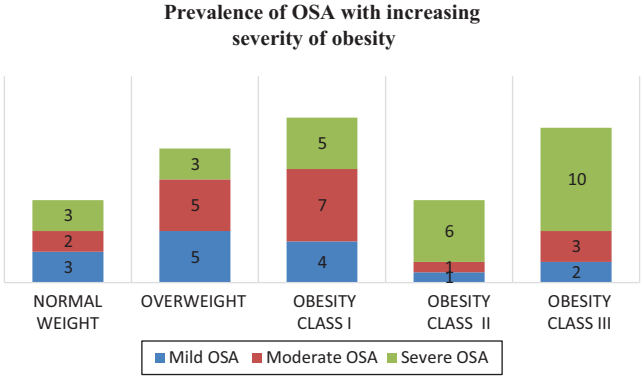

Figure 5. Prevalence of OSA with increasing severity obesity.

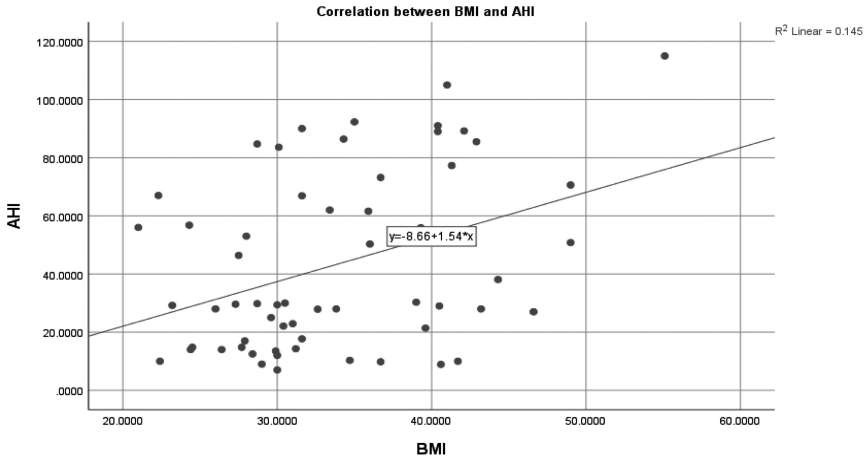

Figure 6. Scattered dot-plot showing positive correlation between BMI and AHI.

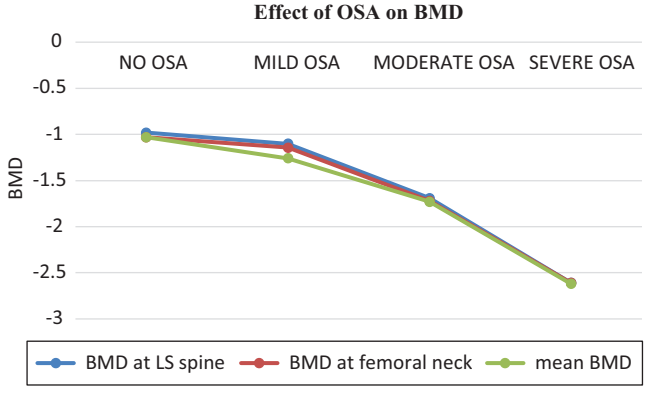

Figure 7. Effect of OSA on BMD at LS spine and femoral neck.

A negative correlation was established between AHI and BMD using Pearson's correlation test ($r = -0.507$, $P < .001$) as depicted in Figure 8.

The results show a significant difference between mean BMD (in T score) in the case group and the control group ((−2.02 ± 1.09) vs. (−1.03 ± 0.97)) using the Student's *t*-test (*t* value = 4.340, $P < .001$, $df = 91$) (Figure 9).

The box-plot in Figure 10 depicts the comparison between the mean BMD (g/cm^2) of males vs. females in both the control and case groups. It was seen that females had lower BMD in both the case and control groups as compared with males in case and control groups (0.815 ± 0.24) versus (0.959 ± 0.26) in the control group whereas (0.783 ± 0.308) versus (0.904 ± 0.308) in cases.

Corelation Between AHI and Vitamin D

With increasing severity of OSA, a decrease in mean serum vitamin D was observed. The mean vitamin D level in the mild OSA group was 24.12 (± 6.27) ng/dL, and moderate level was 20.09 (± 7.55) ng/dL, whereas in the severe group it was 19.89 (± 7.36) ng/dL. The data was statistically significant by applying the ANOVA test ($F = 3.005$, $P < .05$).

A negative correlation using the Pearson correlation test was established between AHI and serum vitamin D level. ($P < .001$, $r = -0.286$) (scattered dot plot in Figure 11).

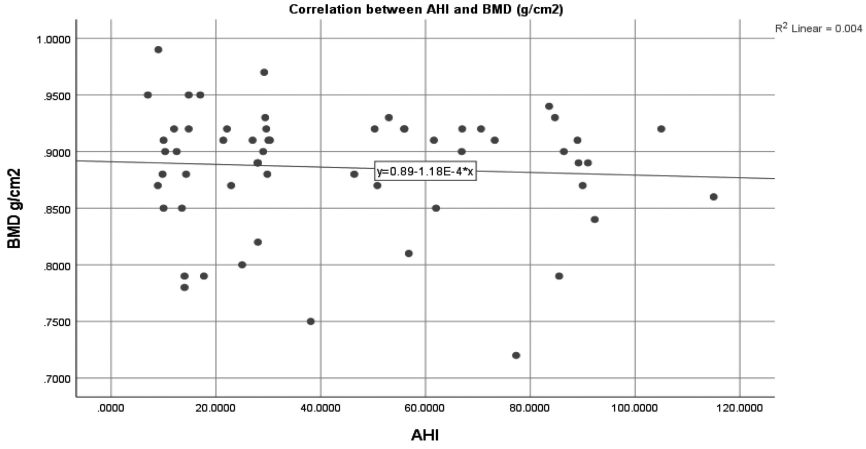

Figure 8. Scattered dot-plot showing negative correlation between AHI and BMD.

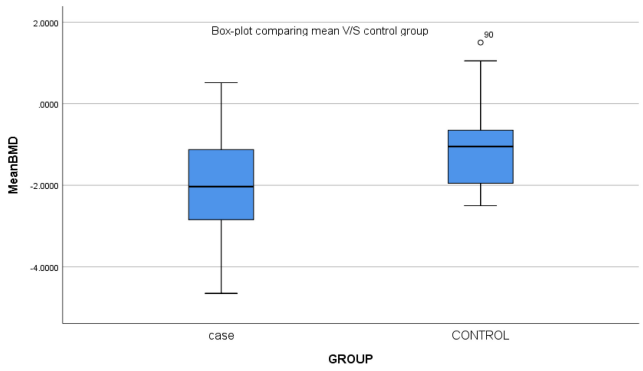

Figure 9. Comparison of mean BMD between cases and controls.

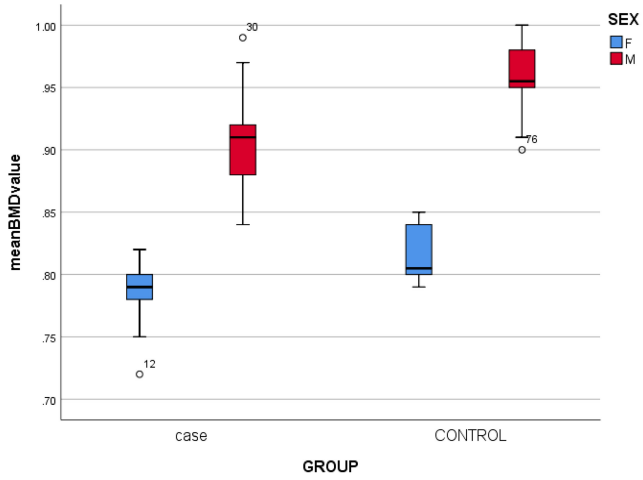

Figure 10. Box-plot showing mean BMD of males and females in the cases and controls group.

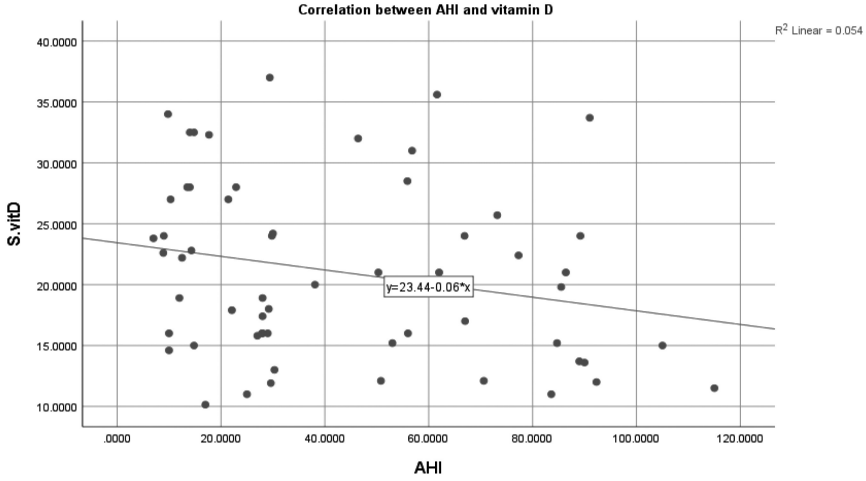

Figure 11. Graph showing negative correlation between AHI and Vitamin D.

Mean vitamin D level in the case group was at a significantly lower level as compared to the control group (21.02 ± 7.27 vs. 24.48 ± 6.92). It also proved to be statistically significant at a *P* value of < 0.05 for *F* statistics (*t* value = 2.246, *P* < .027, *df* = 88). Maximum and minimum values in the control group were 12 ng/dL and 47 ng/dL as compared to 10 ng/dL and 37 ng/dL in the case group (Figure 12).

DISCUSSION

OSA is the most common form of SDB, and many studies have linked OSA to multiple cardiovascular, metabolic, and hormonal disorders, type 2 diabetes mellitus, and insulin resistance inflammatory derangements, but only few studies have investigated the possible relationship between OSA and bone disease and how OSA affects bone metabolism. This study was done to gain insight into the relationship between sleep and bone.

In this study, a total of 59 OSA cases with mean age of 48.029 (± 8.435) years, mean BMI of 33.73 (± 7.48) kg/m^2, mean neck circumference of 37.8 (± 5.08) cm were compared with age, sex and BMI matched 34 non-OSA controls. A related study of similar sample sizes and parameters was done by

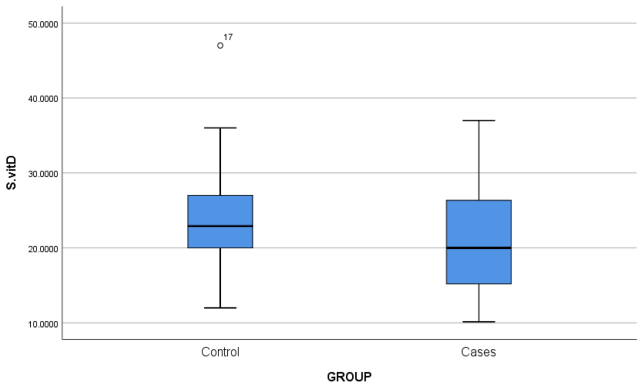

Figure 12. Comparison of mean vitamin D between cases and controls.

Claudio Liguori et al.[17] They compared 92 OSA participants with a sample size of 50 controls (age 51.00 ± 11.68 years, BMI 30.78 ± 1.93 kg/m^2, and ESS score 5.67 ± 2.29) with cases and controls matched for age and BMI. Tomiyama et al.[18] also did a case–control study with a comparable study population. Therefore, we believe that our study's demographic findings are consistent with the literature.

This study contained a population in the age group between 30-60 years. The maximum number of participants were between 41-50 years (39.8%) followed by 51-60 years (33.3%) and 31-40 years (26.9%), which shows that OSA is more prevalent in the older age group. Mean AHI was highest in the 51-60 years age group (48.72(± 29.63)) followed by the 41-50 years age group (45.46(± 32.35)) and lowest in the 31-40 years age group (31.08(± 26.5)). The result showed a statistically significant relation between age and AHI suggesting that increasing age could be a risk factor for OSA. Studies done by Ancoli-Israel and coworkers on the prevalence of OSA showed a similar result. The study was conducted using home polysomnography on a probability sample of 427 men and women of 65-95 years of age. OSA, defined as an AHI of 10 or more, occurred in 70% of the men and 56% of the women, approximately 3-fold higher than the prevalence estimates for OSA in middle age.[19] Bixler and coworkers found that in both men and women those aged 65-100 years o had a prevalence of OSA that was approximately twice higher than (95% CI) OSA prevalence at middle age.[20] Similar results were shown in the Sleep Heart Health Study, by Duran et al. and Littner et al., which supported the hypothesis that age could be a risk factor for OSA.[21-23] There is controversy, however, regarding the occurrence and significance of OSA in older people and in middle-aged people as mentioned by Udwadia et al.[24]

Our study included 78 males (83.9%) and 15 females (16.1%) of mean age 48.94 (± 8.52) and 42.89 (± 5.9), respectively. All females taken in the study were premenopausal and had lower mean AHI than males; however, the data was not statistically significant and hence we suggest that AHI is independent of gender. However, most of the population-based studies have estimated sex-specific prevalence of almost 2- to 3-fold greater risk for men compared with women.[25] Other studies done on epidemiology of OSA are by Mark et al. and Young et al. who have also suggested higher prevalence in males than in females.[21,26,27] The hypothesis for this disparity focuses on the role of sex hormones in OSA pathogenesis. Waldron et al. have shown that sex-based phenotypes including physical features, occupational and other environmental exposures, health behavior, clear sex differences in upper airway shape and genioglossal muscle activity, craniofacial morphology, and pattern of fat deposition have been proposed to account for a higher male risk of OSA.[28] The possible explanation for this disparity in this study could be unequal distribution of gender in the study population. Also only premenopausal females are included in the study due to which most of the females are between 35 and 45 years while in males it is extended upto 60 years of age.

The maximum number of severe OSA participants were in the obesity class III group, followed by obesity class II, class I, overweight, and then normal weight groups. It suggests that OSA is more prevalent in the obese population and with increasing severity of obesity, frequency of severe OSA occurrence increases. A positive correlation was established between AHI and BMI ($r = 0.434$, $P < .05$). Shlomo et al. in his journal says that the incidence of OSA among morbidly obese patients is 12- to 30-fold higher than in the general population.[29] A similar study has been done by Peppard et al. in 690 randomly selected patients over 4 years, and they found that a 10% weight gain predicted an approximate 32% increase in AHI and 10% weight loss predicted a 26% decrease in AHI.[30] A 10% increase in weight predicted a 6-fold increase in the odds of developing moderate to severe SDB. Huang et al. also found similar results.[31] They studied 334 patients and found an AHI of 28.8 ± 21.1/h for males and 18.0 ± 17.7/h for females in normal weight patients, 34.3 ± 23.2/h for males and 23.2 ± 20.3/h for females in overweight patients, and 50.3 ± 29.7/h for males and 27.1 ± 25.2/h for females in obese patients ($P < .001$). Comparable results were obtained in the male group in this study as well. However, the relation between obesity and AHI could not be established in the female group possibly due to the abovementioned limitation. Ancoli-Israel et al. studied the changes in BMI and found that these changes were weakly associated with changes in AHI.[19]

On comparing the BMD of OSA cases with age, sex, and BMI matched non-OSA controls, statistically significant lower BMD values were obtained in the case group as compared to control group. On comparing means in different classes of severity of OSA, we found that there was a decrease (more negative value) in mean BMD with increasing severity of OSA. A statistically negative correlation was established

between AHI and BMD. One cross-sectional study done by Uzkeser et al. evaluated 21 male participants with OSA syndrome and 26 control subjects and found significant differences between OSA participants and control subjects with regard to lumbar L1-L4 BMD and femoral neck BMD values.[32] Tomiyama et al. were the first to report a link between OSA and abnormal bone metabolism. They studied bone metabolic abnormalities in 50 participants with OSA syndrome and 15 controls and found that bone resorption markers (urinary C-terminal telopeptide of type I collagen) were significantly higher in OSA participants compared with control subjects.[18] Although they did not assess BMD, their study suggested a possible association between OSA and osteoporosis. Chakhtoura et al. reported a case of 41-year-old man who presented with bilateral ninth rib fractures and was found to have OSA and osteoporosis and concluded that OSA can lead to bone loss.[33] Other studies have also reported similar results.[17,34,35] Some studies even reported that OSA may be associated with preserved BMD in an older population.[36,37] A possible explanation for this was given by Carreras et al.[38] that recurrent transient falls in oxygen saturation could mobilize mesenchymal stimulating cells capable of undergoing differentiation into osteocytes, resulting in promotion of osteoblastic activity which might slow bone resorption and consequently decrease the risk of osteopenia/osteoporosis related to aging. A population-based cohort study done in Taiwan found that the incidence of osteoporosis was 2.7 times higher in patients with OSA than that in age- and gender-matched controls, after adjusting for medical comorbidities, geographical area, and monthly income.[39] On comparing mean the BMD of males vs. females in the case group, it was seen that females had lower BMD 1.93(± 1.06) versus 2.15(± 1.12). However, the data were not statistically significant. No study so far has compared the effect of OSA on BMD in age and BMI matched males and females. Sforza et al.[36] studied both males (41.1%) and female (58.9%) in their study population. However, both the genders were separately compared with the control group.

In this study, the mean vitamin D level in the case group was significantly lower compared to the control group. A negative correlation was established between AHI and serum vitamin D level. Liguori et al.[17] in his study compared data between groups and documented that OSA patients showed significantly lower vitamin D (18.62 ± 8.02 vs. 31.64 ± 15.03, $P < .0001$). Upala et al.[40] conducted a meta-analysis and a systematic review of almost 11 published observational studies to evaluate the association between OSA and low serum vitamin D levels and confirmed the same. Chen et al.[41] found in his study that serum 25-hydroxy vitamin D level was significantly lower in women with increasing OSA severity. Other studies show a similar association between OSA and vitamin D.[11,42-44] However, the study by Salepci et al.[45] evaluated 195 patients for OSA with a mean age of 49 (± 12) years and BMI of 31 (± 6) kg/m^2 and did not find any association between vitamin D levels and apnea-hypopnea index or BMI.

LIMITATIONS

The main limitation of the study was obesity itself, which is associated with both OSA and BMD loss. In a case–control study it is very difficult to establish an association between OSA and BMD independent of BMI. The study population was too small as the duration of the study was limited and also it was a single-centered study. We did not have a chance to combine our data as the other centers had different polysomnography devices. Gender distribution in case and control groups was not even as there were 84% males while there were only 16% females, and this disparity was due to age limitation in females as only premenopausal females were included in the study. Age distribution between males and females was also not comparable due to the same reason. The maximum age of females taken in the study was 49 years while males were up to 60 years of age. Physical activity assessment, duration of OSA, and lot of other confounding factors which could be directly or indirectly a factor in itself affecting BMD were not properly matched between case and control group.

SUMMARY

- This was a case–control, cross-sectional study conducted at the Department of TB and Respiratory Diseases in collaboration with the Centre of Diabetes, Department of Endocrinology, Aligarh, between the period of December 2017 and September 2019. It aimed to study the effect of OSA on BMD. As serum vitamin D plays a vital role in bone mineralization, the effect of OSA on serum vitamin D was taken as secondary objective.
- The total study population constituted 93 subjects (excluding post-menopausal women, k/c/o osteoporosis, cushing syndrome, Hyper/hypothyroidism, hyperparathyroidism, vitamin D deficiency, diabetes mellitus, liver disease/chronic renal disease, and prolonged use of steroids), of which 59 OSA cases (AHI > 5) with a mean age of 48.02 ± 8.435 years, mean BMI of 33.73 ± 7.48 kg/m^2, mean neck circumference of 37.8 ± 5.08 cm were compared with age, sex, and BMI matched 34 non-OSA (AHI < 5) controls. Cases were further divided into 3 subgroups, namely, mild, moderate, and severe OSA on the basis of AHI, and the results were compared within these groups to establish correlation with increasing severity of OSA. Similar comparisons were made between males and females as well.
- The maximum number of participants were in the middle to older age group. Also an increase in AHI was observed with increasing age. Mean AHI was highest in the 51-60 years age group, followed by 41-50 years group and minimum in the 31-40 years group. Results were not found to be significant when the mean AHI of males and females were compared in the same age group.
- It was found that with an increase in BMI, severity of OSA increases. A positive correlation was established between BMI and AHI.
- The mean BMD in the case group was found to be at a significantly lower side as compared with the control group. A statistically negative correlation was established between AHI and BMD. On comparing the mean BMD of males vs. females in different classes of severity of OSA, it was seen that females had lower BMD.
- Similarly, mean vitamin D level in the case group was significantly at a lower level as compared to the control group. A negative correlation was established between AHI and serum vitamin D level.

CONCLUSION

In this study we found that AHI was inversely correlated with both BMD and serum vitamin D; that is, with increasing severity of OSA, there is a decrease in BMD. Further, as concluded from the study, increasing age and increasing BMI are also risk factors for developing OSA. Hence, as population ages and the prevalence of obesity rises, there is increase in the risk for osteoporosis.

It is therefore important to determine the relationship between these 2 increasingly common diseases, understand the biological processes and establish appropriate screening and interventions to decrease the morbidity, mortality, and costs associated with OSA/osteoporosis so that we may ultimately benefit patients.

Ethics Committee Approval: This study was approved by Ethics committee of Aligarh Muslim University, (Approval No: 20179728).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

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