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ORIGINAL ARTICLE

Studying the Serum Magnesium Level in Adults Patients with Obstructive Sleep Apnea in Baghdad City

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ABSTRACT

Background: *Obstructive Sleep Apnea (OSA) is a significant health problem worldwide. Low magnesium levels may resulted from sleep disorders or deprivation which may worsen the oxidant stress. Nonetheless the effect of OSA on the serum levels of magnesium and other minerals and its health consequences are still not well identified*

Objective: *To assess the level of serum magnesium, calcium, phosphate and albumin in patients with obstructive sleep apnea in comparison to control group and to assess the correlation of these parameters with the severity of disease*

Methods: *A case control study was performed during time period from February to October 2023. The study included a total of 60 subjects (including 30 OSA patients, and 30 non OSA subjects). The OSA groups were further classified according to severity of disease into severe, moderate, and mild OSA.*

Results: *Mean of serum Mg and albumin were significantly lowered in patients with OSA 1.78 mg/dl, 3.81 g/dl respectively, in compare to those without OSA 2.20 mg/dl, 4.39 g/dl with p value < 0.001 to both tests. No significant difference in mean of serum calcium and phosphate between the two groups, p values were 0.81 and 0.61, respectively.*

Conclusion: *The magnesium and albumin levels in OSA patients were significantly low compared to controls, however, no significant changes in these parameters across the OSA severity, other parameters were not significantly different than controls and across severity of disease.*

Keywords: *Obstructive Sleep Apnea, Magnesium, Calcium, Albumin, Phosphate*

1. INTRODUCTION

Obstructive sleep apnea (OSA) is a sleep disorder characterized by recurrent episodes of cessation or significant decrease in airflow in the presence of breathing effort caused by repetitive collapse of the upper airway during sleep. It is the most common sleep-related breathing disorder(1). These episodes are termed "apneas" with complete or near-complete cessation of breathing, lasting for at least 10 s (i.e. airflow restriction by more than 90% according to American Academy of sleep medicine AASM criteria) or "hypopneas" when the reduction in air flow lasting for at least 10 s is partial (as airflow restriction more than 30% according to AASM criteria). The reduction in airflow must be accompanied by a 3% desaturation or an arousal. In either case, a fall in blood oxygen saturation, a disruption in sleep, or both may result (2). The terms obstructive sleep apnea syndrome (OSAS) or obstructive sleep apnea–hypopnea syndrome (OSAHS) may be used to refer to OSA when it is associated with symptoms during the daytime (e.g. excessive daytime sleepiness, decreased cognitive function) (3). According to American Academy of sleep medicine (AASM), OSA is commonly divided into three levels of severity. The severity of OSA is measured by the apnea-hypopnea index (AHI). Apnea-hypopnea index (AHI) is the frequency of apneas and hypopneas per hour of sleep (4).

- Mild OSA: AHI > 5 to < 15
- Moderate OSA: AHI ≥15 to <30
- Severe OSA:AHI ≥ 30

The OSA also classified into adult and pediatric disease. OSA in children differs from adult OSA in its etiology, symptomatology, sleep study findings, and consequences. OSA in the pediatric population is largely caused by increased upper airway resistance during sleep due to soft tissue hypertrophy, craniofacial abnormalities, and/or neuromuscular deficits. The general symptoms of OSA in children are similar to that of adults (snoring and excessive daytime sleepiness), but also manifest as hyperactivity, aggressive behavior, poor school performance, and/or morning headaches (5). Most individuals with OSA are unaware of disturbances in breathing while sleeping, even after awakening. A bed partner or family member may observe an individual snoring or appear to stop breathing, gasp, or choke while

sleeping. Individuals who live or sleep alone are often unaware of the condition. Daytime symptoms include excessive daytime sleep, headaches, fatigue, memory and concentration impairment, poor coordination, anxiety, irritability, and depressed mood (6). These symptoms may be reported during the evaluation of another complaint, detected during health maintenance screening, reported during preoperative screening or as a part of the comprehensive evaluation of patients at high risk for OSA (1). Snoring is the common feature of OSA, it is associated with a sensitivity of 80–90% for the diagnosis of OSA, but its specificity is below 50% (7).

2. METHODOLOGY

Subject

Analytical case-control study that was conducted from February to October 2023 at Baghdad City. The study included 60 Iraqi subjects (30 newly diagnosed OSA cases, and 30 non OSA patients), who did visit the respiratory and otolaryngology center in Baghdad city.

Inclusion Criteria

1. Age between 18 to 70 years old
2. Both males and females
3. Had a body mass index (BMI) of > 27 kg/m²

Exclusion criteria

Patient was excluded if he/she had one or more of the following:

1. Smoking
2. Alcohol consumption
3. Using sedative or muscle relaxant medication
4. Anatomical factors for OSA (micrognathia , retrognathia , tonsillar hyperatrophy, macroglossia, and other factors)
5. Currently using multivitamin or medications that modulate magnesium, calcium, phosphate, and those with disorders known to influence magnesium, calcium, and phosphate metabolism/absorption
6. Parathyroid disease or renal disease.

Diagnosis of OSA and case definition:

Cases of OSA were identified and diagnosed according to American Academy of sleep medicine criteria using PSG and 30 patients were diagnosed and defined as OSA

Ethical approval:

The study was approved by the Ethics Committee of the institution. Informed verbal consent was obtained from all participants and they were informed about the nature of the study, and all who agreed to participate completed a uniform questionnaire.

Study groups:

The subjects in this study were assigned into two groups:

First group: Included 30 patients with confirmed OSA using out of center sleep test (OCST).

Second group: Included 30 non OSA subjects who did not meet criteria for diagnosis OSA.

All the OSA patients who met the inclusion criteria were further subgrouped according to AASM classification into three levels of severity:

Severe OSA: include 13 patients with AHI ≥ 30.

Moderate OSA : include 7 patients with AHI ≥ 15 to < 30.

Mild OSA : include 10 patients with AHI > 5 to < 15.

Collection of blood samples:

Under aseptic procedure, five milliliters of peripheral venous blood were aspirated from the median cubital vein. The syringe samples were pulled in to a clean gel disposable tube for 30 minutes in upstanding position until the blood was clotted, left at room temperature and then centrifuged at (ROTOFIX 32) 4000 revolution per minute(RPM) for 10 minute to obtain serum. Serum was aspirated for immediate measurement of calcium, Albumin, magnesium and phosphate; these were assayed by automated method by Spinreact (spin200).

Statistical Analysis:

The statistical analysis data were analyzed using Statistical Package for Social Sciences (SPSS) version 26. The variables that normally distributed were expressed as means ± SD, while variables that did not normally distributed were expressed as medians with interquartile ranges (IQRs). Independent t-test was used to compare the mean of two groups. Mann-Whitney U test was used to assess the difference between the groups that did not normally distributed, and ANOVA (Analysis of variance) for more than two groups. Pearson's product

moment correlation was applied to study the correlation between study parameters. P. value less than or equal to 0.05 was considered statistically significant.

3. RESULTS

The study included 60 participants were selected to involve 30 OSA diagnosed patients matched with 30 non OSA participants. The OSA patients were further classified into three subgroups according to severity of the disease, the severe OSA subgroup was included 13 patients, moderate subgroup was 7, while the mild subgroup involved 10 patients as shown in (**Figure 1**). Regarding gender distribution, in OSA group, 43.3% of patients were females and 56.7% were males. In non-OSA group, 40% were females and 60% were males, with no significant association between gender and OSA, p value >0.05, as presented in (**Figure 2**). The sleep study parameters, that were obtained from sleep study (appendix) summarized in (**Table 1**) that show comparison of these parameters between two study groups. The median of AHI was 26.5 times/hour (11.75-40.5) was significantly higher in patient with OSA in compare to median in patients without OSA 2.0 times/hour (1-3.25), p value was < 0.001. No significant difference in mean of age and pulse rate, between the groups p value was 0.42, 0.45, respectively. Patients with OSA had significantly higher BMI in compare to those without OSA, p value was < 0.001, while O2 saturation was significantly low in patients OSA in comparison to those without OSA, p value 0.001. Results of biochemical analyses between two study groups expressed in (**Table 2 & Figure 3**). Mean of serum Mg and albumin were significantly lowered in patients with OSA in compare to those without OSA with p value < 0.001 to both tests. No significant difference in mean of serum calcium and phosphate between the two groups, p values were 0.81 and 0.61, respectively. The differences in sleep study parameters between OSA subgroups (mild, moderate, severe) showed in (**Table 3**). A significant difference in mean of AHI when compare OSA subgroups, p value < 0.001, while no significant difference in mean of age with the severity of OSA. There were a statistical significant differences in means of BMI, pulse rate and O2 saturation between the three subgroups of severity of OSA, p values were 0.003, 0.03, 0.002 respectively. In this study biochemical results were used to compare OSA subgroups, and show its changes with severity as expressed in (**Table 4 & Figure 4**). A significant difference in median of vitamin D according to severity, p value 0.03, while there was no significant difference in mean of Mg,

albumin, calcium, and phosphate between OSA subgroups, p values were 0.1, 0.11, 0.71 and 0.66, respectively.

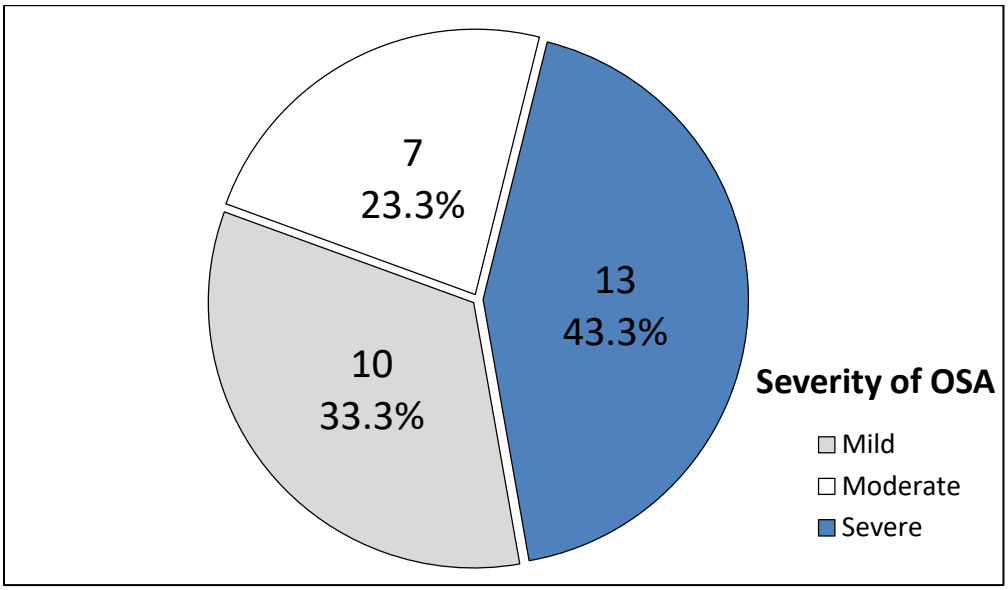

Figure 1. Distribution of patients according to severity of OSA

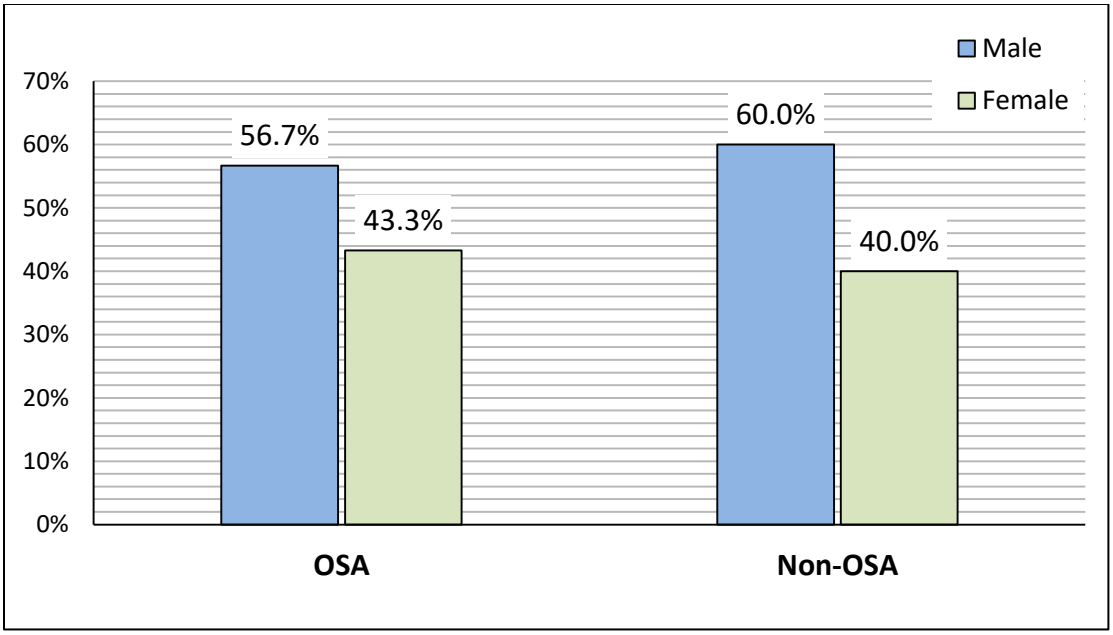

Figure 2. Gender distribution of the studied groups

Table 1. Comparison of AHI, age, BMI, pulse rate, O2 saturation in the two groups.

Parameters	OSA Mean ± SD	Non OSA Mean ± SD	P. value
AHI (Times/hour)	26.5 (11.75-40.5)	2.0 (1-3.25)	< 0.001
Age (Years)	52.13 ± 12.16	49.17 ± 14.89	0.42
BMI (Kg/m^2)	35.76 ± 3.82	32.21 ± 2.23	< 0.001
Pulse rate (Beat/min)	77.60 ± 11.42	75.27 ± 12.33	0.45
O_2 saturation(%)	93.23 ± 2.07	95.03 ± 1.92	0.001

Table 2. Comparison of Mg, albumin, Ca and Phosphate in the two groups

Parameters	OSA Mean ± SD	Non OSA Mean ± SD	P. value
Vitamin D	18.5 ± 4.26	24.0 ± 5.13	0.003
Mg (mg/dl)	1.78 ± 0.34	2.20 ± 0.37	< 0.001
Albumin (g/dl)	3.81 ±0.53	4.39 ± .60	< 0.001
Ca (mg /dl)	9.39 ± 0.61	9.43 ± 0.39	0.81
Phosphate (mg /dl)	3.28 ± 0.64	3.2 ± 0.56	0.61

Table 3. Comparison of AHI, age, BMI, pulse rate, O2 saturation between OSA subgroups.

Parameters	Mild OSA Mean ± SD	Moderate OSA Mean ± SD	Severe OSA Mean ± SD	P. value
AHI (Times/hour)	10.40 ± 2.11	22.14 ± 5.36	43.15 ± 8.21	< 0.001
Age (Years)	48.40 ± 13.53	51.43 ± 14.84	55.38 ± 9.32	0.400
BMI (Kg/m^2)	33.00 ± 3.05	35.42 ± 3.10	38.07 ± 3.37	0.003
Pulse rate (Beat/min)	72.10 ± 9.92	74.43 ± 10.69	83.54 ± 10.72	0.03
O_2 saturation(%)	94.70 ± 1.88	93.57 ± 1.71	91.92 ± 1.60	0.002

Table 4. Comparison of Mg, albumin, Ca and Phosphate between OSA subgroups.

Parameters	Mild OSA Mean ± SD	Moderate OSA Mean ± SD	Severe OSA Mean ± SD	P. value
Mg (mg/dl)	1.95 ± 0.35	1.82 ± 0.23	1.64 ± 0.34	0.10
Albumin (g/dl)	4.01 ± 0.49	3.96 ±0.57	3.58 ± 0.49	0.11
Ca (mg /dl)	9.52 ± 0.76	9.27 ± 0.45	9.37 ± 0.59	0.71
Phosphate (mg /dl)	3.27 ± 0.63	3.47 ± 0.22	3.19 ± 0.80	0.66

4. DISCUSSION

The pathogenesis of OSA is multifactorial for this reason this study was conducted to study the level of some parameters in a sample of Iraqi adults group diagnosed with OSA and compare to (age and BMI) matched non OSA participants, and study its relation to degree of severity. Severe OSA was overrepresented (43,3%) compared to mild (33,3%) and moderate (23,3%), reflecting the demographic of respiratory centers and clinic population. Males percentage was overexpressed in two study groups, but this gender variation was not significant, in contrast to Kerley, et al.(8) who found significant male overexpression in OSA disease. The age profile was similar in two groups (OSA and non OSA), also no significant variation with the severity. As expected PSG variables were show significant difference between OSA and non OSA group (apart from pulse rate) also across OSA severity subgroups. The AHI showed strong significant difference between two groups and increase with severity as this the main principle for diagnosis of OSA and for classify OSA into subgroups according to AASM. Regarding BMI this study was demonstrated strong relation between diagnosis of OSA and BMI, and strong positive correlation with severity of disease, this was expected as obesity and central fat distribution one of common non anatomical risk factors for development of the disease (9,10). Pulse rate was not significantly higher in OSA patients vs. matched non OSA group, while it is significantly increase with severity of disease, this agree with Kerley, et al. (8). On contrary, this study revealed significant decrease in O2 saturation in OSA patients compared to normal, together with significant decrease with severity. This was in concordance with Kerley, et al. (8)

In the study by Lu et al. (11), HIF-1α serum levels were increased in severe OSA patients compared with mild and moderate OSA and control subject. HIF-1α expression was positively correlated with AHI, and it was negatively correlated with mean and minimum oxyhaemoglobin saturation during sleep (11). The difference in serum Mg between OSA patients and control group revealed that the mean value of serum Mg was significantly low in OSA patients (1,78 mg/dl) compared to non OSA (2.20 mg/dl), this finding is consistent with a systemic review and metanalysis done by Al Wadee et al. (12), while disagree with Cakir et al. (13). When comparing serum Mg with different OSA severities, current study found that despite decrease in mean of serum Mg in severe compared to moderate and

mild OSA, this difference is not statistically significant. This consistent with Zota et al. (14) who showed that severe OSA patients had reduced serum Mg levels when compared to those with moderate OSA, but the mean difference was not statistically significant. Additionally, in multiple regression analysis, Karamanli et al. (15) found that the serum Mg level was still significantly associated with AHI after adjusting for age, gender, and BMI. However, the direct relationship between OSA and serum Mg levels is complex and multifactorial. It is still unclear whether OSA directly causes a lower serum Mg level or whether the lower serum Mg level is one of the risk factors in OSA. Factors suggested to impact serum Mg levels in OSA patients include oxidative stress, insufficient dietary intake, and impaired Mg regulation due to other comorbidities (12). In a recent clinical study of patients with type 2 diabetes, a condition often associated with OSA, hypomagnesaemia was seen to be a significant pathogenic factor that causes increased oxidative stress. Mg deficiency was seen to enhance oxidate stress marker and was shown to have a significant negative correlation with serum malondialdehyde, an indicator of oxidative stress (16). Furthermore, intermittent nocturnal hypoxia was also significantly associated with oxidative stress, increased pro-inflammatory markers, and OSA, according to Orrù et al. (17). Other studies have suggested that disturbances of trace mineral metabolism were due to oxidative stress and inflammatory response. OSA affects the absorption and circulating levels of these substances (18). In this study, serum Ca and P levels were not considerably different between the two study groups, nor with severity of OSA, this agree with Ayhan eta al. (19). Albumin had been measured in this study in order to adjustment measured calcium, but it showed significant decrease in its mean in OSA patients group (3.81 g/dl) compared to non OSA group (4.39 g/dl). No significant changes was appeared in its mean with the severity of the disease. Faulx et al. (20) demonstrated that severe OSA is independently associated with increased urine albumin excretion, a marker of both endothelial dysfunction and cardiovascular disease risk. This study provides further evidence supporting the hypothesis that sleep apnea-related pathophysiology independently contributes to systemic cardiovascular risk.

5. CONCLUSIONS

Magnesium and albumin levels in OSA patients were significantly low compared to controls, however, no significant changes in these parameters across the OSA severity, other parameters were not significantly different than controls and across severity of disease.

Ethical Approval:

All ethical issues were approved by the author. Data collection and patient's enrollment were in accordance with Declaration of Helsinki of World Medical Association, 2013 for the ethical principles of researches involving human. Signed informed consent was obtained from each participant and data were kept confidentially.

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