

# OBSTRUCTIVE SLEEP APNEA SYNDROME IN PATIENTS WITH CUSHING'S SYNDROME

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## OBJECTIVES

Diabetes mellitus and obesity are well known risk factors associated with obstructive sleep apnea syndrome (OSAS). Cushing's syndrome (CS) is characterised by centripetal obesity and diabetes mellitus. Centripetal pattern of fat accumulation also involves the neck, including parapharyngeal spaces, face and trunk. Skeletal muscle weakness may decrease the activity of the genioid and genioglossus muscles, which contribute to stabilize the upper airways. All these features may be associated with the pathogenesis of OSAS in patients with CS (1, 2). OSAS has been studied rarely in patients with Cushing's syndrome. We investigated the possible association between CS and OSAS in this study.

## METHODS

Thirty female patients diagnosed with Cushing's syndrome (CS) between January 2014 and August 2015 in the department of Endocrinology and Metabolism of Ondokuz Mayıs University Medical School and 30 female obese control subjects were included in this study. Twenty four of patients had ACTH-secreting pituitary microadenoma and 6 had cortisol-secreting adrenal adenoma. CS was excluded from all control subjects. Patients with ectopic CS, alcoholism, depression or glucocorticoid treatment were excluded from the study. All the participants were evaluated by polysomnography. A standard overnight PSG (Embla® 54500, UK) had been performed on all participants. The apneas and hypopneas were identified and scored according to the American Academy of Sleep Medicine Task Force (AASM) criteria (3). The apnea-hypopnea index (AHI) was defined as the total number of obstructive apneas and hypopneas per hour of sleep. OSAS was defined as AHI of  $\geq 5$  events/hour. Severity of OSAS was classified as mild (AHI  $\geq 5$  and  $< 15$  events per hour of sleep), moderate (AHI  $\geq 15$  and  $< 30$  events per hour of sleep), severe (AHI  $\geq 30$  events per hour of sleep), and No-OSAS (AHI  $< 5$  event per hour of sleep). Body mass index (BMI) of the subjects was recorded and insulin resistance were calculated by HOMA score. The study was approved by the ethics committee of Ondokuz Mayıs University and informed consent was obtained from all subjects.

## RESULTS

The median age and BMI of patients with CS and control subjects were similar. Although the median fasting insulin levels were similar, both the median fasting glucose and HOMA score and AHI were higher in patients with CS compared to the control obese subjects (Table 1-2) (Figure 1). Fifty percent of patients with CS and 23.3 % of control subjects had OSAS (Table 2). There was a positive correlation between AHI and HOMA scores ( $r=0.281$ ,  $p=0.046$ ). Twenty (66.6%) out of 30 patients with CS and 12 (40%) out of 30 control subjects had glucose intolerance. Those who has glucose intolerance, 8 (40%) with CS and 6 (50%) controls had OSAS. Furthermore, all subjects with AHI  $\geq 15$  had glucose intolerance. Polysomnographic data as well as the subjective sleepiness score are shown in Table 2.

Table 1: Clinical characteristics of the patients (n=30) and control obese subjects (n=30).

| Characteristics          | Cushing's Syndrome |          | Control Group |         | P Value |
|--------------------------|--------------------|----------|---------------|---------|---------|
|                          | Median             | Range    | Median        | Range   |         |
| Age (years)              | 45.8               | 19-64    | 44            | 23-63   | 0.567   |
| BMI (kg/m <sup>2</sup> ) | 32                 | 25-45    | 33            | 21-45.9 | 0.583   |
| AHI (events/hour)        | 5                  | 2-16     | 1.35          | 0-17.7  | 0.005   |
| HOMA score               | 2.7                | 1.2-14.8 | 2.35          | 2-10.2  | 0.046   |
| Fasting glucose (mg/dL)  | 109                | 68-159   | 96            | 69-149  | 0.028   |
| Fasting insulin (mIU/L)  | 11.6               | 5-46     | 8.65          | 1-32    | 0.117   |

AHI, Apnea-Hypopnea Index; BMI, Body Mass Index

Table 2: Polysomnographic data as well as the subjective sleepiness score in patients with Cushing's syndrome (n=30) and control obese subjects (n=30).

| Characteristics            | Cushing's Syndrome | Control Group | P value |
|----------------------------|--------------------|---------------|---------|
| AHI (events/hour)          | 5 (2-16)           | 1.35 (0-17.7) | 0.005   |
| AHI $\geq 5$ (% with OSA)  | 50                 | 23            | 0.003   |
| AHI $\geq 10$ (% with OSA) | 13.3               | 6.6           | 0.300   |
| AHI $\geq 15$ (% with OSA) | 3.3                | 6.6           | 0.550   |

Data are median. AHI, Apnea-Hypopnea Index, OSA, Obstructive Sleep Apnea.

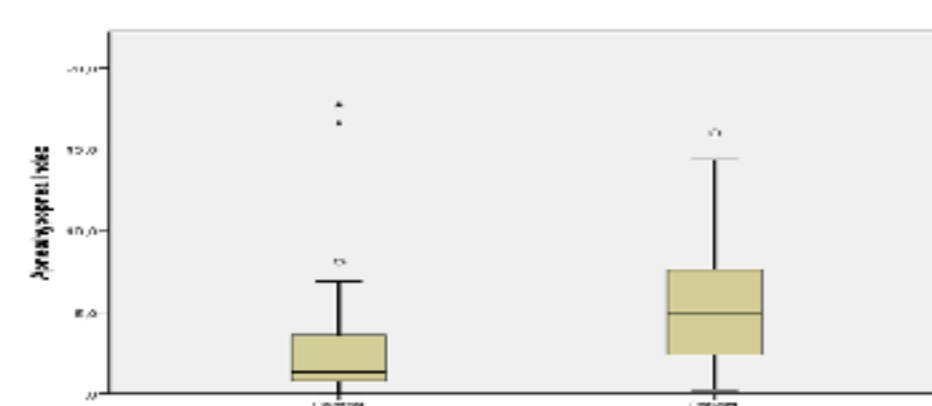


Figure 1. Apnea-Hypopnea Index was higher in women with Cushing's syndrome compared to control obese subjects (5 vs.1.35,  $p=0.005$ ).

## CONCLUSIONS

The risk of OSAS increased in patients with CS, compared to control subjects with similar age and BMI. Insulin resistance may have a meaningful role for this increment. The possible role of muscle weakness, hypercortisolemia and centripetal pattern of fat accumulation for developing OSAS should be investigated in appropriately designated studies. CS is a strong risk factor for OSAS. Therefore CS should be excluded in patients with OSAS and vice versa.

## References

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