ORIGINAL ARTICLE

Association of Hypothyroidism in Obstructive Sleep Apnea Syndrome

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Abstract

Background: Hypothyroidism and obstructive sleep apnea syndrome (OSAS) are common comorbid conditions with overlapping clinical presentation. We decided to study the association of hypothyroidism in our OSAS patients.

Methodology: This observational study included 108 patients with clinical features suggesting OSAS. The clinical details were noted; Polysomnography (PSG) and thyroid function tests (TFT) were done. Qualitative and quantitative data was analyzed with appropriate tests.

Results: Seventy-two (66.7%) men and 36 (33.3%) women were included. PSG confirmed OSAS in 78 (72.2%). The severity of OSAS was mild, moderate, severe in 30 (38%), 28 (36%), 20 (26%) respectively. Thirteen (12%) had hypothyroidism; subclinical in 2 (15%) and clinical in 11 (85%). Only 2 (15%) were on optimal medical treatment. Hypothyroidism was seen in 11(14%) of OSAS, against in 2(7%) of the non-OSAS group. OSAS was found in 11(85%) of hypothyroid, against in 67 (71%) of the Euthyroid group. A statistically significant association between OSAS and hypothyroidism treatment was observed.

Conclusion: The prevalence of hypothyroidism was higher in OSAS; though statistically insignificant. Association between OSAS and hypothyroidism treatment was statistically significant.

Keywords: Apnea-hypopnea index (AHI), Polysomnography, Thyroid function tests (TFT), OSAS, Hypothyroid treatment.

Introduction

Obstructive sleep apnea syndrome (OSAS) is an increasingly prevalent chronic condition which is still under diagnosed. It is a peculiarity of this noisy disease that it announces itself to everyone within earshot - except its victims. The intermittent hypoxemia and sleep fragmentation caused by recurrent episodes of upper airway collapse are chiefly responsible for the pathophysiology associated with this condition[1]. Hypothyroidism is a common endocrine disorder resulting from a deficiency of thyroid hormone[2]. Unfortunately, OSAS and hypothyroidism can easily be confused. Obesity, fatigue, decreased libido, depressed mood, and impaired concentration are symptoms common to both disorders. Even snoring, which is a prominent presenting complaint with OSAS, has been observed universally within at least some hypothyroid patients. Periorbital and peripheral edema are usually associated with hypothyroidism but are also frequently

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seen in patients with OSAS. Because the two disorders have been estimated to occur together, the sleep respiratory clinic environment can be an opportunity for misdiagnosis. This study was conducted to analyze the association of hypothyroidism in patients with OSAS.

Methodology

An observational hospital study was conducted at a tertiary care center after institutional ethic committee permission from 2011 to 2013, for the duration of 2 years. Adult patients presenting with clinical features suggestive of OSAS were included in the study. The demographic data, history, examination findings were noted. Each patient was then subjected to a Polysomnography (PSG). PSG was performed using Alice PDx device (Philips Respironics, Murrysville, PA). It is a portable Type II or III diagnostic device designed to record physiologic variables during sleep. Type II devices are portable and offer at least seven channels which include oxygen saturation, at least two airflow/effort channels, electrocardiogram (ECG)/heart rate (HR), electrooculogram (EOG), and chin electromyogram (EMG). Type III devices record at least four signals and include oxygen saturation, at least two airflow/effort channels, and ECG/HR. All patients were evaluated with thyroid function tests (TFT) and ultrasound of neck for goiter. TFT included measurement of thyroid stimulating hormone (TSH), free triiodothyronine (fT3) and free thyroxine (fT4). Subsequently, they were assessed on the satisfaction of the diagnostic criteria for OSAS & Hypothyroidism.

Qualitative data was analyzed with frequencies and percentages. Parametric correlation between AHI and all other variables were calculated. Pearson Chi-Square, Continuity Correction & Fisher's Exact Test were applied to study the association between OSAS prevalence, severity, and prevalence of hypothyroidism and the impact of hypothyroidism therapy.

Results

One hundred and eight patients with clinical features suggestive of OSAS were enrolled in the study. Of these, 72 (66.7%) were men and 36 (33.3%) were women. The age ranged from 18 years to 76 years with the mean age of 52.52 years. The PSG confirmed OSAS in 78 (72.2%) and in the rest 30 patients (27.8%) OSAS was ruled out as per the American Sleep Disorders Association (ASDA) Standards of Practice Committee guidelines. Mean TSH was 3.65mIU/L and mean AHI was 19.56/hr. The average of various variables among the cases is enumerated in Table-1. There was no statistically significant correlation was found between AHI and TSH (p-value = 0.342) nor between AHI and FT3 (p-value = 0.4434) (Table-2).

Out of the 78 patients (the OSAS group), the severity of OSAS was found to be mild in 30 (38%), moderate in 28 (36 %) and severe in 20 (26%). Based on the TFT, 13 patients (12%) were found to have hypothyroidism. Out of these 13 (the Hypothyroid group), the severity of Hypothyroidism was found to be Subclinical in 2 (15%) and Clinical in 11 (85%) patients. Of the Hypothyroid group, 2 patients (15%) were found to be on optimal medical treatment and the remaining 11 (85%) were either newly diagnosed or were on sub-optimal therapy. Out of the total 108 patients, 5 (4.6%) had goiter. The remaining 103 patients (95.4%) did not have any enlargement of thyroid gland on USG neck. Based on the PSG and the TFT, 11 patients (10.0%) were found to have both OSAS and hypothyroidism and in the OSAS group (78 patients), hypothyroidism was found to be present in 11 (14%) and absent in 67 (86%). Thus the prevalence of hypothyroidism in OSAS was 14%. In the non-OSAS group (30 patients), hypothyroidism was found to be present in 2 (7%) and absent in 28 (93%) patients. Thus the prevalence of hypothyroidism in non-OSAS was 7%. Of the Hypothyroid group (13 patients), OSAS was found to be present in 11 (85%) and absent in 2 (15%). Thus the prevalence of OSAS in hypothyroidism was 85%. Of the 95 euthyroid patients, OSAS was found to be present in 67 (71%) and absent in 28 (29%). Thus the prevalence of OSAS in euthyroid patients was 71%. No statistically significant association was found between OSAS prevalence and severity with hypothyroidism and vice versa. However, there was a statistically significant association between OSAS prevalence & hypothyroidism treatment (p value <0.05) (Table 3).

Discussion

OSAS and hypothyroidism are two prevalent health problems of adult population. OSAS is characterized by recurrent episodes of upper airway collapse during sleep, leading to intermittent hypoxemia and sleep fragmentation. Patients with OSAS often present with

Table 1: Average of Various Variables Among the Cases

Variables	Mean	SD	Median	IQR	Mode	Minimum	Maximum
Age (yrs)	52.52	11.92	54.00	12.75	51.00	18.00	76.00
FT3 (pmol/L)	7.93	3.86	8.61	5.43	1.40	0.90	16.70
FT4 (pmol/L)	7.03	2.98	7.86	4.05	5.60	0.90	12.20
TSH (mIU/L)	3.65	4.95	2.69	2.43	0.37	0.13	35.65
AHI (/hr)	19.56	22.37	10.50	22.80	1.00	1.00	98.00

Table 2: Parametric Correlation Between AHI and Thyroid Function Tests

Variables		Age (yrs)	FT3 (pmol/L)	FT4 (pmol/L)	TSH (mIU/L)	AHI (/hr)
Age (yrs)	**Pearson Correlation**	1	-0.092	-0.051	0.065	0.069
	p-value		0.3456	0.5987	0.5049	0.4758
FT3 (pmol/L)	**Pearson Correlation**	-0.092	1	.470(**)	-0.054	-0.075
	p-value	0.3456		**2.84E-07**	0.582	0.4434
FT4 (pmol/L)	**Pearson Correlation**	-0.051	.470(**)	1	-0.046	0.044
	p-value	0.5987	**2.84E-07**		0.6356	0.654
TSH (mIU/L)	**Pearson Correlation**	0.065	-0.054	-0.046	1	0.092
	p-value	0.5049	0.582	0.6356		0.342
AHI (/hr)	**Pearson Correlation**	0.069	-0.075	0.044	0.092	1
	p-value	0.4758	0.4434	0.654	0.342	
**** Correlation is significant at the 0.01 level (2-tailed) * Correlation is significant at the 0.05 level (2-tailed)**						

Table 3: Association Between OSAS and Hypothyroidism Treatment

OSAS		Hypothyroidism			Total
		Treated #	Non-treated #	Normal	
Yes	No.	0	11	67	78
	%	0.0%	14.1%	85.9%	100.0%
No	No.	2	0	28	30
	%	6.7%	0.0%	93.3%	100.0%
Total	No.	2	11	95	108
	%	1.9%	10.2%	88.0%	100.0%
Chi-Square tests	**Value**	**df**	**p-value**	**Association is-**	
Pearson Chi-Square $	9.567	2	0.008	Significant	
Pearson Chi-Square #	0.538	1	0.463	Not significant	
Fisher's Exact Test #			0.509	Not significant	
$ 3 cells (50.0%) have expected count less than 5. # Column data pooled & Chi-Square Test reapplied.					
^ Continuity Correction applied. 1 cell (25.0%) is expected to have a count of less than 5. A p-value of Fisher's Exact Test will be used.					

symptoms of excessive daytime somnolence, fatigue, lassitude & lethargy, all of which can be seen in individuals with another common disorder such as hypothyroidism. Differentiation between the two disorders is difficult as hypothyroid patients are also at risk for secondary sleep-disordered breathing (SDB). Other respiratory complications that occur in some hypothyroid individuals include upper airway obstruction (secondary to goiter), obesity, respiratory myopathy, and blunted ventilatory chemosensitivity. Each of these complications can contribute to SDB. Obesity, airway obstruction, and altered ventilatory chemosensitivity also occur in primary OSAS.

The first case reporting an apneic episode in a patient with myxoedema was published in 1964[3]. Following that, many studies[1, 3-14] have investigated further the prevalence of hypothyroidism in OSAS and vice versa. The prevalence of hypothyroidism in patients evaluated by PSG for OSAS is 0.7-3.4%, depending on the upper limit set for normal TSH, gender, and age distribution of the studied samples[6-9]. Kapur et al reported a prevalence of 1.4% of subclinical hypothyroidism in OSAS and this association was greater in females and those less than 50 years of age[9]. In a group of Taiwanese patients with OSAS, a prevalence of 3.1% was reported despite using higher TSH level (>25 mIU/l) to define hypothyroidism[6]. The prevalence is also not significantly different in patients highly suspected to have OSAS(1.5%) than those already diagnosed to have OSAS by overnight sleep study (2.4%)[10]. Winkelman and co-workers also reported a prevalence of 1.6% in patients suspected to have OSAS and 2.9% in those confirmed to have OSAS[8]. Other studies have reported a much higher prevalence. In a study of 78 overweight and obese adult patients referred to a sleep clinic, a prevalence rate of 11.5% was reported[11]. Females with OSAS have been reported to have higher rates of undiagnosed than diagnosed hypothyroidism[8,15]. Some of the previous studies defined hypothyroidism as the presence of a high serum thyroid-stimulating hormone (TSH) level without commenting on thyroxine hormone level. This means that some of the patients thought to have hypothyroidism may actually have had subclinical hypothyroidism, which carries different therapeutic and prognostic implications[8, 9, 16, 17]. In a recent study, Bahammam et al[18] reported the prevalence of newly diagnosed clinical hypothyroidism as 0.4%, and the prevalence of newly diagnosed subclinical hypothyroidism as 11.1% in OSAS. In the non-OSAS patients, the prevalence of newly diagnosed clinical hypothyroidism was reported as 1.4% and the prevalence of newly diagnosed subclinical hypothyroidism as 4%[18]. The authors had concluded that the prevalence of newly diagnosed clinical hypothyroidism was low; however, subclinical hypothyroidism was common among patients with OSAS. In lieu of the uncertainty of the benefit achieved by treating subclinical hypothyroidism, the authors recommended not to perform routine thyroid function testing for OSAS patients[18]. Overall, the prevalence of clinical hypothyroidism in patients diagnosed with OSAS or referred to sleep centers with a clinical suspicion of OSAS is not higher than the prevalence in the general population. The prevalence of hypothyroidism in OSAS was 14% in our study. If we compare it with previously reported studies, it was on the higher side but nearly equals the prevalence reported by Resta O et al[11]. Older age and increased BMI are well-established risk factors for both hypothyroidism & OSAS. The higher prevalence of hypothyroidism in our study may be due to these confounding factors. Though the prevalence of hypothyroidism was 14% in the OSAS group and 7% and in the non-OSAS group, there was no statistically significant association between OSAS & hypothyroidism which was consistent with previously reported studies.

Limited data are available about the prevalence of OSAS in hypothyroid patients[6,19-28]. The incidence is estimated to range from 25-82%. Most of the obtained data are from case reports and case series, and their findings are variable. In a study of 50 patients with primary hypothyroidism, 30% were found to have OSAS[19]. These patients had overt severe hypothyroidism as manifested by TSH levels and symptoms. For milder cases and subclinical cases, the prevalence might be less. The variability in the results is influenced by the characteristics of the studied group. The predominance of male gender can result in a higher prevalence of OSAS as it is one of the main risk factors for OSAS. In smaller studies, a higher prevalence has been reported[20]. In our study, of the 108 patients, 13 (12%) were hypothyroid and 95 (88%) were euthyroid. The severity of hypothyroidism was found to be subclinical in 2 (15%) and clinical in 11 (85%). Only 2 patients (15%) were found to be on optimal medical treatment. The prevalence of OSAS was 85% in the hypothyroid group and 71% and in the euthyroid group.

Theoretically, replacing thyroid hormone should reverse most if not all the complications associated with the state of deficiency. However, in clinical practice,

this is not absolutely correct. Changes such as respiratory muscle weakness can be reversible with thyroxine therapy. Difficult weaning in hypothyroid patients can be facilitated with thyroxine therapy too and mechanical obstruction due to thyroid goiter can be reverted with thyroidectomy. However, OSAS response to thyroxine therapy is variable[6,19,20,26,27]. In a series of nine hypothyroid patients with OSAS(AHI range 17-176/hour), thyroxine therapy improved the outcome. Six of them were obese and had the higher range of AHI and showed significant improvement in AHI after 3-12 months of thyroxine therapy despite no improvement in weight[20]. Another series of 5 patients with OSAS who received thyroxine therapy, showed a significant reduction in AHI after 4 months of therapy; however, snoring persisted and required a longer duration of therapy to improve[6]. Snoring refers to upper airway resistance and the longer duration required to improve it is basically related to the duration needed to resolve or improve upper airway changes induced by hypothyroidism. In a larger group of patients, Resta O and co-workers[22] divided patients into 3 groups: group-A: 63 patients with normal thyroid function, group-B: 30 patients affected with subclinical hypothyroidism and treated with levothyroxine for at least 2 years and group-C: 15 patients with TSH >4miu/l and not treated with levothyroxine[22]. The prevalence and severity of OSAS did not differ between the three groups and levothyroxine therapy did not influence OSAS outcome in patients with subclinical hypothyroidism. It was also noticed that levothyroxine therapy in patients with subclinical hypothyroidism and OSAS was associated with less daytime sleepiness as measured by the ESS when compared to the untreated group[22]. Untreated subclinical hypothyroidism by itself is a known cause of EDS (excessive daytime sleepiness) measured both subjectively and objectively, which improved with thyroxine therapy[23]. On the other hand, the outcome of treating primary hypothyroidism with levothyroxine in patients with OSAS has resulted in a significant improvement in AHI within 7-11 months of therapy. This improvement was accompanied by significant reduction in BMI, skinfold thickness, pedal edema, and other biochemical markers[19]. However, in the same study, two patients had missed the follow-up and both failed to show any improvement in OSAS following levothyroxine therapy, thought to be due to the overweight that did not reduce with therapy[19]. Failure to improve OSAS by achieving euthyroid state suggests that hypothyroidism is not the only factor and there are other factors playing a role in causing OSAS. It is also thought that thyroid hormone deficiency results in long-term changes in the upper airway and thus an improvement in OSAS lags behind even after achieving the euthyroid state[24]. Furthermore, it is the treatment of the severe forms of hypothyroidism (myxoedema) that improves the concomitant OSAS[23]. Based on the available evidence, thyroxine cannot be considered as the only therapeutic option for OSAS in patients with hypothyroidism, especially in elderly and those with cardiovascular diseases[25]. In our study, OSAS was found to be present in all 11 (100%) patients in the newly diagnosed or sub-optimal treated hypothyroid group, whereas it was found to be present in 0 (0%) patients in the optimally treated hypothyroid group. Thus the prevalence of OSAS was 100% in the newly diagnosed or sub-optimal treated hypothyroid group and 0% in the optimally treated hypothyroid group. Thus, we found that patients with OSAS often had undiagnosed or sub-optimally treated hypothyroidism but the difference in its prevalence in OSAS patients was not statistically significant when compared to patients who were not found to have OSAS. However, the population of hypothyroid patients in this study was small which may have influenced the results.

Limitations of the study include selection bias and small sample size, especially of the hypothyroid group. This may have influenced the statistical power of the determination of an independent association between OSAS and hypothyroidism. Hence, a study with a larger sample size is required to show that the difference in prevalence of hypothyroidism in OSAS and non-OSAS patients is statistically significant.

Conclusions

The prevalence of hypothyroidism was found to be higher in patients with OSAS than in those without OSAS; however, this difference was not found to be statistically significant. But, there was statistically significant association between OSAS and hypothyroidism treatment. Thus all patients with OSAS should be assessed and evaluated for hypothyroidism as it helps in an appropriate treatment with CPAP or thyroid supplements or both.

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