ORIGINAL RESEARCH ARTICLE

Usefulness of Checking Sensitization Status in Adult Patients with Suspected Sleep Apnea

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Abstract

Aim: An association between obstructive sleep apnea (OSA) and allergic rhinitis (AR), both common with increasing prevalence worldwide, has frequently been reported. The objective of this study was to assess acceptability, feasibility, and usefulness of routinely checking sensitization status in suspected sleep apnea.

Materials and methods: All consecutive adult patients referred to an adult sleep clinic in Malta over a 10-week period were included. A medical history, physical examination, and skin testing for common aeroallergens were performed for all and rhinoconjunctivitis quality of life questionnaire (RQLQ), Total-4-nasal symptom score (T4NSS), and visual analogue scale (VAS) for AR patients. Uncontrolled AR was treated. The polysomnography report was reviewed.

Results: Our cohort included 95 patients—34.7% were sensitized and diagnosed with AR. The most common perennial aeroallergens were *Dermatophagoides pteronyssinus* (86.1%), farina (75%), seasonal aeroallergens, tree (19%), and grass pollen (19%). When comparing allergic and nonallergic groups, the former were younger ($p = 0.002$), more likely female ($p = 0.06$) and asthmatic ($p = 0.014$), suffered rhinorrhea ($p = 0.02$), or other rhinoconjunctivitis symptoms ($p < 0.001$). Patients with AR were less likely diagnosed with sleep apnea (60.6%) compared to those without (81.3%) ($p = 0.014$). A total of 54.2% of patients with normal polysomnography were diagnosed with AR compared to 30% of sleep apnea patients ($p = 0.26$).

Conclusion: Skin prick testing (SPT) in this context is acceptable, safe, and feasible, mainly useful in younger females, asthmatics, and those with AR symptoms. Diagnosing AR in patients whose symptoms have been mistaken for sleep apnea and in patients with coexisting sleep apnea will improve morbidity and quality of life.

Clinical significance: Checking sensitization status in patients with suspected sleep apnea will improve clinical outcomes.

Keywords: Adult, Obstructive sleep apnea, Prevalence.

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Introduction

Obstructive sleep apnea (OSA) is highly prevalent worldwide.[1–5] Obesity is the most common risk factor[1,3] together with an aging population.[6] Allergic rhinoconjunctivitis is a chronic, immunoglobulin E (IgE)–mediated inflammation[7] following inhalation of airborne allergens[8] with varying adult prevalence rates globally[9–12] of growing major health concern[11,13] and a significant impact on quality of life (QOL).[13–22] It is often undiagnosed[23] and associated with sleep disturbance.[8,14,23,24]

The coexistence of OSA and allergic rhinitis (AR) has frequently been studied[25–27] though the precise underlying pathophysiological mechanisms are unclear.[28] Such patients report increased stress and fatigue.[29] AR-induced fatigue and daytime somnolence may mimic OSA.[28] Several studies on AR patients report a higher OSA prevalence[15,30,31] and worse polysomnographic parameters.[30,32] AR increases the risk of developing OSA by increasing airway resistance.[27,33,34] AR-induced nasal congestion results in a higher OSA prevalence[35,36] though controversial.[37–39] Studies on OSA patients revealed that AR had an effect on symptoms, but not on polysomnographic results.[28,39,40] Neither was AR a risk factor for OSA.[28,40,41] In a local study, no association was identified with AR.[43] Treating AR, namely intranasal steroids, may improve OSA symptoms.[39,41,42] Poorly controlled AR may contribute to poorer continuous positive airway pressure (CPAP) compliance.[44] Knowing the patients' allergic status is deemed important when investigating sleep-disordered breathing (SDB).[34,45,46] The Adult OSA Quality Measures Workgroup mentions input from various specialists.[35] Checking patients' sensitization status is useful to distinguish AR from nonallergic rhinitis (NAR)[24,47] when treating[24] and recommending allergen avoidance.[48] Skin prick testing (SPT) is safe,[24] reliable, minimally invasive, and inexpensive[49,50] and provides immediate results.[51]

No studies have investigated the usefulness of performing SPT routinely in patients with suspected OSA. The primary objective was to identify and compare phenotypic characteristics based on sensitization status. Secondary objectives included identifying SPT reactivity patterns and assessing the prevalence of AR in patients in whom OSA is excluded.

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Materials and Methods

All adult English-speaking, mentally competent patients referred consecutively to the respiratory department for suspected OSA at Mater Dei Hospital over a 10-week period referred to a domiciliary sleep study for suspected OSA were asked to participate in this cross-sectional analytic cohort study. Patients were excluded if any of these criteria were met: under the age of 18, absolute contraindications to perform a SPT—history of collapse or a severe reaction to SPT or severe/uncontrolled asthma or pregnancy, previous surgery to the nose and/or rhinosinusal surgery, and inability or unwillingness to provide written consent.

The questionnaire included demographic details, a medical history, and an epworth sleepiness score (ESS). A disease-specific questionnaire, rhinoconjunctivitis quality of life questionnaire (RQLQ) was used to measure QOL for patients with a diagnosis of AR. Another two tools were utilized to assess AR severity—visual analogue scale (VAS) and Total-4-nasal symptom score (T4NSS). Treatment was prescribed if patients had uncontrolled AR symptoms. A second visit (Visit 2) was organized 8 weeks later for all participants during which the sleep study result was recorded, and the questionnaire was repeated.

Patients with rhinitis symptoms were referred to an ear, nose, and throat (ENT) specialist for a comprehensive assessment. Diagnosis of AR was based on the allergic rhinitis and its impact on asthma (ARIA) guidelines, the presence of symptoms, and a positive SPT.[8] Symptoms included a combination of rhinorrhea, nasal obstruction, nasal itching, and sneezing in the presence/absence of eye symptoms. Severity was classified according to the effect of AR on sleep disturbance, impairment of daily activities, leisure and/or sport, impairment of work, and troublesome symptoms. Impairment of one or more was diagnosed as moderate to severe AR while impairment of none was classified as mild AR.[8]

Patients with symptomatic AR, partially treated or untreated, were prescribed treatment with intranasal corticosteroids (NCS) and oral antihistamines (OAH) as per the ARIA guidelines.[8]

Polysomnography studies were conducted in all recruited participants at the sleep laboratory of Mater Dei Hospital by trained sleep physiologists. Using polysomnography equipment (Nox T3 Technologies–Cardinal Health®), physiological measurement data were acquired. Staging was performed according to the criteria of the American Academy of Sleep Medicine (AASM)'s manual for sleep scoring version-2 (2012). An obstructive apnea was defined as cessation of airflow nasal pressure for at least 10 seconds. An obstructive hypopnea was defined as a 50% reduction in nasal pressure for at least 10 seconds, compared with baseline, in combination with arousal or oxygen desaturation of at least 3%. apnea–hypopnea index (AHI) was defined as the mean number of obstructive apneas and hypopneas per hour of sleep. OSA severity was defined as follows—mild: AHI 5–15/hour, moderate: AHI 15–30/hour, and severe: AHI $\geq$ 30/hour.[52]

Data were analyzed using the statistical package for social sciences (SPSS®) version 26. A $p < 0.05$ was taken to be statistically significant. Ethical approval was obtained from the Malta University Research Ethics Committee, Malta, prior to the commencement of the study (FRECMDS_1819_095).

Results

During the 10-week study period, 132 patients were referred, of whom 95 (72%) patients fulfilled the inclusion criteria and agreed to participate. Twenty patients (15%) refused participation. Seventeen patients (12.9%) did not meet the eligibility criteria. Our cohort included 51 males (53.7%) with a mean age of 49 $\pm$ 13 years. The mean BMI was 34.9 $\pm$ 7.5 kg/m^2.

Rhinoconjunctivitis symptoms were reported in 61 patients (64.2%) with only 34 patients (35.8%) having no rhinitis symptoms at all. The most common rhinitis symptoms were as follows: nasal blockage 54 (56.8%), nasal itching 33 (34.7%), and rhinorrhea 27 (28.4%). Thirty-two (33.7%) patients complained of allergic eye symptoms.

Reported symptoms associated with sleep apnea in all participants ($n = 95$) were as follows: snoring 86 (90.5%), daytime somnolence 70 (73.7%), unrefreshed sleep 58 (61.1%), headaches 36 (37.9%), witnessed apneic episodes 35 (36.8%), memory loss 13 (13.7%), and poor concentration 12 (12.6%). Analysis of domiciliary sleep studies revealed that sleep apnea was diagnosed in 70 patients (74.7%) of the cohort recruited and the majority suffered mild (42.2%, 40 patients) or severe disease (31%, 29 patients).

Thirty-six (37.9%) patients were sensitized to at least one aeroallergen. There were no adverse events during or following the SPT. Only three patients were sensitized without ever having rhinoconjunctivitis symptoms and were therefore excluded from further analysis. The majority of the patients (63.6%) were diagnosed with moderate to severe AR and 18 patients (54.5%) were diagnosed with persistent disease. The mean ($\pm$SD) baseline results for all AR patients were as follows: VAS 4.2 $\pm$ 2.9 mm, T4NSS 3.6 $\pm$ 3.8, and RQLQ 1.9 $\pm$ 1.7.

OSA was diagnosed in 61 patients (64.2%). The incidence of OSA was nonsignificantly higher in the mild AR group ($p = 0.2$), and there was no significant difference in OSA severity between AR groups ($p = 0.68$) according to the AR severity (Table 1).

Comparison between allergic and nonallergic patients at baseline in terms of demographic data is shown in Table 2, whereas Table 3 compares symptoms, sleep indices, and 36-item Short Form Survey (SF-36) domains between allergic and nonallergic patients.

Table 4 compares AR patients with or without OSA. When comparing patients without OSA to patients with OSA (Table 5), AR was diagnosed in 54.2% of the former group and approximately 30% in the group of patients with OSA ($p = 0.26$).

The majority of the patients with mild disease (83.3%) and moderate to severe AR (77.3%) were not receiving any regular ARIA-recommended medication. Untreated patients with moderate to severe persistent AR ($n = 18$) treated for 8 weeks were analyzed. Two patients admitted to not starting treatment prescribed for AR. T4NSS at baseline improved from 4.6 $\pm$ 4.5 to 4 $\pm$ 2.3 ($p = 0.6$). VAS at baseline improved from 6.1 $\pm$ 1.7 to 5 $\pm$ 2.5 ($p = 0.14$). RQLQ domains improved significantly throughout apart from the non-nose/eye symptoms ($p < 0.01$).

Discussion

This study was carried out to evaluate the acceptability and usefulness of performing SPT in adult patients referred to suspected sleep apnea. The coexistence of sleep apnea and allergic conditions has frequently been described.[25–27] Despite recent sleep guideline recommendations stating that diagnostic polysomnography should be carried out following a comprehensive clinical evaluation,[53] there is a failure to include an allergy history or allergy testing. Awareness has been raised that many AR sufferers are undiagnosed and unaware of their disease[54] and a survey in 11 European countries has emphasized the emotional burden, daily restrictions, and the negative impact on QOL.[54] Results of a web-based survey

Table 1: Comparison of demographic data and sleep parameters according to AR severity ($n = 33$)

	Mild (n = 12)	*Moderate to severe (n = 21)*	*p value*
Mean age (±SD), years	47.3 (11.8)	40.2 (12.8)	0.12
Males, *n* (%)	5 (41.7)	9 (40.9)	**<0.001**
Mean baseline VAS (±SD)	1.1 (1.4)	5.9 (1.9)	**<0.001**
Mean T4NSS baseline (±SD)	1.8 (2)	4.5 (4.2)	**0.02**
Mean baseline RQLQ	0.38 (0.79)	2.7 (1.5)	**<0.001**
Mean BMI, kg/m^2	36.1 (8.5)	32 (9)	0.2
ESS	3.8 (3.6)	8.9 (4.3)	**0.002**
Mean (±SD)			
OSA diagnosis yes, *n* (%)	9 (75)	11 (52.4)	0.2
AHI (events per hour), mean (±SD)	17.7 (22.9)	22.5 (34.9)	0.68
ODI (events per hour), mean (±SD)	17.9 (22.1)	19.9 (32.3)	0.89
Nocturnal O_2 saturation, mean (±SD)	93 (1.6)	91.2 (9.6)	0.4
Lowest O_2 desaturation, mean (±SD)	78.8 (9.3)	85 (9.7)	0.09
OSA severity, *n* (%)			
Mild	5 (55.5)	4 (36.4)	0.16
Moderate	2 (22.2)	3 (27.3)	0.6
Severe	2 (22.2)	4 (36.4)	0.64

A *p*-value <0.05 is clinically significant

Table 2: Comparison of demographic data between allergic and nonallergic patients

Demographic data	*Allergic (n = 33)*	*Nonallergic (n = 59)*	*p value*
Mean age (±SD), years	42.8 (12.7)	52.8 (12.8)	**0.002**
Median age, years	43	52	
Males, *n* (%)	14 (42.4)	37 (62.7)	0.06
Smoking status, *n* (%)			
Current/previous	12 (36.4)	25 (42.4)	0.57
Never	21 (63.6)	34 (57.6)	
Employment status, *n* (%)			
Employed	19 (57.6)	36 (61)	**<0.001**
Unemployed/retired	14 (42.4)	23 (39)	
Alcohol, *n* (%)			
Social	31 (93.9)	56 (94.9)	0.71
Regular (>7 units per week)	2 (6)	3 (5)	
Pet ownership, *n* (%)	18 (54.5)	30 (50.8)	0.73
Mean BMI, kg/m^2	33.7 (8.9)	35.6 (6.7)	0.18
Comorbidities, *n* (%)			
Hypertension	5 (15.2)	19 (32.2)	0.1
Asthma	14 (42.4)	11 (18.6)	**0.014**
Psychiatric	3 (9)	12 (20.3)	0.1
Hyperlipidemia	2 (6)	11 (18.6)	0.14
Diabetes mellitus	1 (3)	8 (13.5)	0.15
Hypothyroidism	0	8 (13.5)	**0.02**

A *p*-value <0.05 is clinically significant

recommend that allergists are involved in the diagnosis and management of SDB.[25] It is recommended that general practitioners, respiratory, allergy, and ENT (ear, nose, and throat) specialists are made aware of the AR and sleep disorder relationship.[15] To the best of our knowledge, no conclusive data on the importance of routinely checking sensitization status of all patients referred to the possible sleep apnea have been published so far.

SPT was well tolerated in all our patients and acceptability was 72%. SPT was chosen since results are available more rapidly compared to serum IgE levels. The aeroallergen panel utilized was similar to that available at our local hospital, in line with European recommendations. Fifteen percent of patients refused participation as they were not interested in SPT due to the absence of allergic symptoms. This suggests that the prevalence

Table 3: Comparison of symptoms and sleep indices between allergic and nonallergic patients

	Allergic (n = 33)	*Nonallergic (n = 59)*	*p value*
OSA symptoms, *n* (%)			
Snoring	30 (90.9)	52 (89.7)	0.86
Daytime somnolence	23 (69.7)	44 (75.9)	0.61
Apneic episodes	14 (42.4)	19 (32.8)	0.34
Headaches	13 (39.4)	21 (36.2)	0.72
Unrefreshed sleep	22 (66.7)	32 (55.2)	0.31
Memory loss	5 (15.2)	7 (12)	0.4
Poor concentration	7 (21.2)	3 (51.7)	**0.04**
AR symptoms, *n* (%)			
Rhinorrhea	15 (45.5)	12 (20.3)	**0.02**
Nasal obstruction	29 (87.9)	24 (40.7)	**<0.001**
Sneezing	21 (63.6)	12 (20.3)	**<0.001**
Eye symptoms	19 (57.7)	13 (22)	**<0.001**
ESS, mean (±SD)	7.1 (4.7)	8.1 (5.6)	0.4
OSA diagnosis yes, *n* (%)	20 (60.6)	48 (81.3)	**0.014**
AHI (events per hour), mean (±SD)	20.8 (30.8)	24.7 (26.8)	0.54
ODI (events per hour), mean (±SD)	19.2 (28.7)	23.1 (25.7)	0.52
Nocturnal O_2 saturation, mean (±SD)	91.9 (7.6)	92 (3.6)	0.97
Lowest O_2 desaturation, mean (±SD)	82.8 (9.6)	77.4 (11)	**0.02**
OSA severity, *n* (%)			
Mild	9 (45)	19 (39.6)	0.55
Moderate	5 (25)	13 (27)	0.42
Severe	6 (30)	16 (33.3)	0.27

A *p*-value <0.05 is clinically significant

Table 4: Comparison of AR patients (*n* = 33) with or without OSA

	OSA (n = 20)	*No OSA (n = 13)*	*p value*
Mean age (±SD), years	44.9 (13.5)	39.6 (11.3)	0.24
Males, *n* (%)	11 (55)	3 (23)	0.06
ESS			
Mean (±SD)	6.4 (4.9)	8.2 (4.3)	0.25
OSA symptoms, *n* (%)			
Snoring	20 (100)	10 (76.9)	0.08
Daytime somnolence	11 (55)	3 (23.1)	**<0.001**
Apneic episodes	10 (50)	0	0.07
Headaches	6 (30)	7 (53.8)	0.19
Unrefreshed sleep	10 (50)	12 (92.3)	**<0.001**
Memory loss	2 (10)	4 (30.7)	0.18
Poor concentration	5 (25)	2 (15.3)	0.51
AR symptoms, *n* (%)			
Rhinorrhea	7 (35)	8 (61.5)	0.15
Nasal obstruction	18 (90)	11 (84.6)	0.67
Sneezing	11 (55)	10 (76.9)	0.2
Eye symptoms	9 (45)	10 (76.9)	0.07
Mean baseline VAS (±SD)	3.9 (3)	4.5 (3)	0.6
Mean T4NSS baseline (±SD)	3.1 (3.4)	4.1 (4.3)	0.46
Mean baseline RQLQ	1.4 (1.5)	2.1 (1.7)	0.31

A *p*-value <0.05 is clinically significant

of sensitized cases (37.9%) in this cohort is overestimated since the majority of these patients are unlikely to be sensitized.

The most prevalent aeroallergen in our local cohort was house dust mite (HDM)-*Dermatophagoides pteronyssinus* (European HDM) (86.1%) or *Dermatophagoides farina* (American HDM) species (75%) or both (69.4%). We tested only these species since they are the most predominant and important[8] and probably the most researched.[55] HDM allergy is the leading cause of respiratory allergic

Table 5: Comparison of characteristics based on OSA severity

	No (n = 24)	*Mild (n = 30)*	*Moderate (n = 19)*	*Severe (n = 22)*	*p value*
Mean age (±SD), years	45.1 (12.6)	51.2 (13.1)	53.1 (14.2)	46.6 (13.1)	0.14
Males, *n* (%)	7 (29.2)	12 (40)	15 (78.9)	17 (77.3)	**<0.001**
Mean BMI, kg/m^2	30.1 (6.7)	34.2 (7.1)	35.8 (6.1)	40.6 (6.6)	**<0.001**
ESS	7 (4.5)	6.3 (4.4)	9.8 (5.5)	8.6 (6.6)	0.11
Mean (±SD)					
Symptoms of OSA					
Snorer	19 (79.2)	27 (90)	18 (94.7)	21 (95)	0.1
Apnea	4 (16.7)	9 (30)	9 (47.4)	13 (59)	**<0.001**
Sleepiness	20 (83.3)	21 (70)	14 (73.7)	15 (68.2)	0.45
Headaches	11 (45.8)	14 (46.7)	4 (21.1)	7 (31.8)	0.15
Memory loss	5 (20.8)	3 (10)	5 (26.3)	0	0.22
Decreased concentration	3 (12.5)	2 (6.7)	6 (31.6)	1 (4.5)	**0.01**
Unrefreshed sleep	17 (70.8)	18 (60)	11 (57.9)	12 (54.5)	0.77
AHI (events per hour), mean (±SD)	/	8.5 (3.1)	20.7 (3.7)	66.1 (27)	**<0.001**
ODI (events per hour), mean (±SD)	/	7.9 (4)	18 (4.1)	63 (24.2)	**<0.001**
Nocturnal O_2 saturation, mean (±SD)	/	93.1 (2)	92.5 (1.6)	87.3 (9.2)	**<0.001**
Lowest O_2 desaturation, mean (±SD)	/	79.8 (8.1)	79.2 (7.3)	68.9 (11.7)	**<0.001**
Symptoms of AR					
Rhinorrhea	11 (45.8)	5 (16.7)	4 (21.1)	6 (27.2)	0.1
Nasal obstruction	20 (83.3)	16 (53.3)	10 (52.6)	7 (31.8)	**0.01**
Nasal itching	13 (54.1)	8 (26.7)	3 (15.8)	8 (36.3)	**0.04**
Conjunctivitis	13 (54.1)	9 (30)	3 (15.8)	7 (31.8)	**0.04**
AR diagnosis					
Total *n* (%)	13 (54.2)	10 (33)	5 (26)	6 (27.3)	0.26
Mild *n* (%)	3 (23)	5 (50)	2 (40)	2 (33.3)	0.86
Moderate to severe *n* (%)	10 (77)	5 (50)	3 (60)	4 (66.7)	0.1
NAR diagnosis					
Total *n* (%)	9 (38)	8 (26.7)	5 (26.3)	5 (22.7)	0.07

A *p*-value <0.05 is clinically significant

disease worldwide,[56] with prevalence estimated between 18 and 30% though this varies geographically.[55] Humidity is critical for HDM indoors and outdoors, with higher concentrations found in damp houses.[55] The annual average relative humidity in Malta is high, averaging 75%, up to 80% in December,[57] around the time of recruitment, potentially explaining our high HDM sensitization prevalence.

The most common seasonal aeroallergens were tree mix and olive pollen equally (19%). Olive trees are widely cultivated in Malta. Cypress pollen allergy, though not the most prevalent in our cohort (13.9%), is found frequently in the Mediterranean. Our patients with intermittent allergic rhinitis (IAR) were asymptomatic or mildly symptomatic since the study was not performed during the pollen season. Mould allergy was rarely present despite our humid climate.[57]

Not all subjects demonstrating an IgE-mediated immune response have symptoms.[13] We diagnosed clinically irrelevant sensitization in three patients (8.3%). It is reported to occur to a single aeroallergen in 1–5% and in 8–30% to a panel of aeroallergens.[58] Knowing such results is important to provide advice, given to our affected patients, to avoid progression to allergic disease since prospective studies have estimated that 30–60% eventually become allergic.[58]

In our study, we aimed to identify phenotypic characteristics of patients being referred to sleep studies and receiving allergy testing. Phenotypes are defined as "a category of patients distinguished from others by a single or combination of disease features, in relation to clinically meaningful attributes."[59] Evidence has shown that AHI alone is insufficient for diagnosing and managing OSA. In addition to molecular phenotyping, clinical phenotyping is recommended based on symptoms and comorbidities, anatomical and/or physiological features, and OSA severity.[59] AR phenotypes have been described based on gender, age, disease severity, duration, seasonality, symptomatology, allergic triggers, and response to treatment.[47] We identified that allergic patients were significantly younger ($p = 0.002$), more likely to be female ($p = 0.06$) and asthmatic ($p = 0.014$), when compared to nonallergic patients, suggesting that these patients are more likely to benefit from skin testing to common aeroallergens. AR symptoms were all significantly more prevalent in the allergic group ($p < 0.05$).

A large proportion of our allergic patients were diagnosed with OSA (60.6%) but less than nonallergic patients (81.3%) despite similar ESS ($p = 0.4$). Some studies suggest that AR worsens OSA.[12] It is reported that OSA was more prevalent in AR patients than healthy controls[15] but our controls were not all healthy for comparison. A study revealed that 23.3% of AR patients are at high risk for OSA,[27] lower than other studies—36%[60] and 32.7%[41] while a meta-analysis including 44 studies ($n = 6086$) reported 22.8%.[26] Our cohort

showed a higher prevalence, but our referrals had symptoms of OSA in addition, some of which are similar to AR. Both AR and NAR have been identified as risk factors for OSA in a small study ($n = 48$).[60] No such predominance in OSA severity was identified when comparing allergic and nonallergic groups. OSA prevalence was higher in IAR than persistent allergic rhinitis (PAR), 80 vs 44.4% ($p < 0.001$) who also had a higher AHI ($p = 0.04$) despite having lower ESS ($p < 0.001$). When compared to healthy controls, patients with PAR had worse polysomnographic parameters including sleep efficiency, arousal index, average and lowest oxygen saturations, and snoring time although AHI was not significantly different.[60] Observed pathologic differences in sleeping parameters could not be elucidated apart from a significantly lower oxygen desaturation in the nonallergic patients.

A third of our patients with OSA were diagnosed with AR, similar to a study ($n = 112$) on polysomnography-diagnosed OSA in whom 33% were diagnosed with AR.[29] An increased prevalence of AR among patients with OSA is commonly reported—35.2% and[26] 28.7%.[28] Just like our findings, AR presence was not influenced by OSA severity. A previous study by the investigator identified no association between OSA and AR, but allergy was diagnosed using the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaires without formal allergy testing.[60] However, AR was more prevalent in patients without OSA (54.3%, $p = 0.26$), especially moderate to severe AR ($p = 0.1$), as was NAR (38%, $p = 0.07$), unlike a recent similar Saudi Arabian study ($n = 157$), in whom AR was diagnosed in 52.6% of OSA individuals, not significantly different from the non-OSA individuals.[39] As expected, rhinoconjunctivitis symptoms were all more common in the group without OSA, especially nasal obstruction ($p = 0.01$), nasal itching ($p = 0.04$), and conjunctivitis ($p = 0.04$).

Patients with untreated moderate to severe persistent AR were prescribed regular NCS and OAH (ARIA recommendations)[8] to be used as needed. NCS are the most effective AR medications, especially for nasal congestion,[14] and are well tolerated with few reported adverse effects.[8] For patients to adhere to the treatment prescribed, they must be convinced that the treatment is beneficial and outweighs possible side effects,[20] thus emphasizing the need to educate our patients. RQLQ domains showed significant improvement apart from non-nose/eye symptoms.

The major strengths of this study are that we present innovative data that should improve management in adults referred to sleep clinics. The investigator was blinded to the results of the sleep studies, hence reducing bias. The vast majority of our patients had uncontrolled and untreated AR, so the effects of drugs on sleep and polysomnographic parameters were excluded. Since the whole study was carried out in the off-pollen season, seasonal aeroallergen exposure was not a confounding factor.

Our study included several limitations. A limited panel of allergens may indicate that testing may have missed some important allergens, especially in symptomatic nonsensitized individuals. However, our panel choice overall mirrored that available in routine clinical practice. The limited number of patients limited by the duration of the study meant that statistical analysis was not always significantly powered. Asthma was self-reported with no objective investigations performed. Potential confounding factors such as asthma control could have influenced our results. Correlation with asthma control may have provided more accurate results. The inability to translate RQLQ into Maltese introduced bias by excluding patients from lower socioeconomic classes. Our patients were not compared to healthy controls. This implies that QOL impairments may be related to other comorbidities and health issues. Only publications in English were utilized meaning that we may have missed similar international studies. Waiting lists for ENT reviews and the limited availability of naso-endoscopy limited our study since patients could not receive a formal ENT examination. Nasal symptoms may have been attributed to AR instead of an alternative underlying diagnosis. Compliance of prescribed treatment and allergen avoidance was not measured, so changes in RQLQ in treated AR patients were based on presumed compliance.

Conclusion

AR is frequently underdiagnosed and undertreated and is considered a trivial disease, despite our results confirming the negative impact that AR has on QOL. Our findings show that SPT is safe, acceptable, feasible, and useful at our local sleep clinic. HDM allergy should be given the highest priority when dealing with AR patients in this cohort.

The study findings have helped us identify two cohorts of patients needing attention. Firstly, patients whose symptoms on referral were misdiagnosed as possible OSA (normal polysomnography), who were actually suffering from AR. The negative impact of AR on sleep with resultant somnolence, similar to that experienced with OSA, would be a plausible explanation for these referrals to our sleep clinic. Identifying these patients early on could avoid unnecessary polysomnograms while diagnosing and treating AR appropriately without delay. Secondly, our findings highlight that the high prevalence of AR among patients diagnosed with OSA though QOL was not significantly worsened in these patients. Introducing a comprehensive evaluation of allergy-related symptoms during sleep clinics is likely to be beneficial. While OSA treatment has proven to be effective, recognizing and treating both conditions concurrently may improve QOL probably while improving the chances of compliance with CPAP therapy.

Clinical Significance

Our recommendations include the inclusion of SPT for common aeroallergens as a routine evaluation during adult sleep clinic visits particularly to female and younger patients, who complain of AR symptoms and/or suffer from asthma. Optimizing health services with allergist-guided treatment while educating professionals to refer such patients appropriately should reduce morbidity and improve QOL.

References

1. Cistulli PA, Sutherland K. Phenotyping obstructive sleep apnoea-Bringing precision to oral appliance therapy. J Oral Rehabil 2019;46(12):1185–1191. DOI: 10.1111/joor.12857.
2. Patil SP, Schneider H, Schwartz AR, et al. Adult obstructive sleep apnea: pathophysiology and diagnosis. Chest 2007;132(1):325–337. DOI: 10.1378/chest.07-0040.
3. Senaratna CV, Perret JL, Lodge CJ, et al. Prevalence of obstructive sleep apnea in the general population: a systematic review. Sleep Med Rev 2017;34:70–81. DOI: 10.1016/j.smrv.2016.07.002.
4. Bauters FA, Hertegonne KB, De Buyzere ML, et al. Phenotype and risk burden of sleep apnea: a population-based cohort study. Hypertension 2019;74(4):1052–1062. DOI: 10.1161/HYPERTENSIONAHA.119.13452.

5. Heinzer R, Vat S, Marques-Vidal P, et al. Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study. Lancet Respir Med 2015;3(4):310–318. DOI: 10.1016/S2213-2600(15)00043-0.
6. Benjafield AV, Ayas NT, Eastwood PR, et al. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. Lancet Respir Med 2019;7(8):687–698. DOI: 10.1016/S2213-2600(19)30198-5.
7. Bachert C, van Cauwenberge P, Olbrecht J, et al. Prevalence, classification and perception of allergic and non-allergic rhinitis in Belgium. Allergy 2006;61(6):693–698. DOI: 10.1111/j.1398-9995.2006.01054.x.
8. Bousquet J, Khaltaev N, Cruz AA, et al. Allergic rhinitis and its impact on asthma (ARIA) 2008 update. Allergy 2008;63(Suppl. 86):8–160. DOI: 10.1111/j.1398-9995.2007.01620.x.
9. Anastassakis K, Chatzimichail A, Androulakis I, et al. Skin prick test reactivity to common aeroallergens and ARIA classification of allergic rhinitis in patients of Central Greece. Eur Arch Otorhinolaryngol 2010;267(1):77–85. DOI: 10.1007/s00405-009-1065-x.
10. Maspero J, Lee BW, Katelaris CH, et al. Quality of life and control of allergic rhinitis in patients from regions beyond western Europe and the United States. Clin Exp Allergy 2012;42(12):1684–1696. DOI: 10.1111/j.1365-2222.2012.04025.x.
11. Bauchau V, Durham SR. Prevalence and rate of diagnosis of allergic rhinitis in Europe. Eur Respir J 2004;24(5):758–764. DOI: 10.1183/09031936.04.00013904.
12. Valero A, Quirce S, Dávila I, et al. Allergic respiratory disease: different allergens, different symptoms. Allergy 2017;72(9):1306–1316. DOI: 10.1111/all.13141.
13. Bousquet J, Burney PG, Zuberbier T, et al. GA2LEN (Global Allergy and Asthma European Network) addresses the allergy and asthma 'epidemic'. Allergy 2009;64(7):969–977. DOI: 10.1111/j.1398-9995.2009.02059.x.
14. Davies MJ, Fisher LH, Chegini S, et al. A practical approach to allergic rhinitis and sleep disturbance management. Allergy Asthma Proc 2006;27(3):224–230. DOI: 10.2500/aap.2006.27.2858.
15. Léger D, Annesi-Maesano I, Carat F, et al. Allergic rhinitis and its consequences on quality of sleep: an unexplored area. Arch Intern Med 2006;166(16):1744–1748. DOI: 10.1001/archinte.166.16.1744.
16. Sabharwal G, Craig TJ. The effect of rhinitis on sleep, quality of life, daytime somnolence, and fatigue. In: Mahmoudi M, editor. Allergy and asthma: practical diagnosis and management. 2nd ed. US: Springer International Publishing; 2016. p. 87–97.
17. Thompson A, Sardana N, Craig TJ. Sleep impairment and daytime sleepiness in patients with allergic rhinitis: the role of congestion and inflammation. Ann Allergy Asthma Immunol 2013;111(6):446–451. DOI: 10.1016/j.anai.2013.05.020.
18. Colás C, Galera H, Añibarro B, et al. Disease severity impairs sleep quality in allergic rhinitis (The SOMNIAAR study). Clin Exp Allergy 2012;42(7):1080–1087. DOI: 10.1111/j.1365-2222.2011.03935.x.
19. Shariat M, Pourpak Z, Sabetkish N, et al. Evaluation of psychological score and quality of life in adults with allergic rhinitis and assessment of related risk factors. Tanaffos 2017;16(3):233–239. PMID: 29849677. PMCID: PMC5960228.
20. Tatar EC, Sürenoğlu UA, Saylam G, et al. Is there any correlation between the results of skin-prick test and the severity of symptoms in allergic rhinitis? Am J Rhinol Allergy 2012;26(1):37–39. DOI: 10.2500/ajra.2012.26.3750.
21. Bousquet PJ, Demoly P, Devillier P, et al. Impact of allergic rhinitis symptoms on quality of life in primary care. Int Arch Allergy Immunol 2013;160(4):393–400. DOI: 10.1159/000342991.
22. Blaiss MS, Hammerby E, Robinson S, et al. The burden of allergic rhinitis and allergic rhinoconjunctivitis on adolescents: a literature review. Ann Allergy Asthma Immunol 2018;121(1):43–52. DOI: 10.1016/j.anai.2018.03.028.
23. Shedden A. Impact of nasal congestion on quality of life and work productivity in allergic rhinitis: findings from a large online survey. Treat Respir Med 2005;4(6):439–446. DOI: 10.2165/00151829-200504060-00007.
24. Wise SK, Lin SY, Toskala E, et al. International consensus statement on allergy and rhinology: allergic rhinitis. Int Forum Allergy Rhinol 2018;8(2):108–352. DOI: 10.1002/alr.22073.
25. Shusterman D, Baroody FM, Craig T, et al. Role of the allergist-immunologist and upper airway allergy in sleep-disordered breathing. J Allergy Clin Immunol Pract 2017;5(3):628–639. DOI: 10.1016/j.jaip.2016.10.007.
26. Cao Y, Wu S, Zhang L, et al. Association of allergic rhinitis with obstructive sleep apnea: a meta-analysis. Medicine (Baltimore) 2018;97(51):e13783. DOI: 10.1097/MD.0000000000013783.
27. Wongvilairat S, Assanasen P, Banhiran W, et al. The prevalence of high risk of obstructive sleep apnea in patients with allergic rhinitis. Asian Pac J Allergy Immunol 2019;3(10). DOI: 10.12932/AP-141218-0458.
28. Zheng M, Wang X, Zhang L. Association between allergic and nonallergic rhinitis and obstructive sleep apnea. Curr Opin Allergy Clin Immunol 2018;18(1):16–25. DOI: 10.1097/ACI.0000000000000414.
29. Park CE, Shin SY, Lee KH, et al. The effect of allergic rhinitis on the degree of stress, fatigue and quality of life in OSA patients. Eur Arch Otorhinolaryngol 2012;269(9):2061–2064. DOI: 10.1007/s00405-011-1888-0.
30. Kalpaklioğlu AF, Kavut AB. Allergic and nonallergic rhinitis: can we find the differences/similarities between the two pictures? J Asthma 2009;46(5):481–485. DOI: 10.1080/02770900902849897.
31. Canova CR, Downs SH, Knoblauch A, et al. Increased prevalence of perennial allergic rhinitis in patients with obstructive sleep apnea. Respiration 2004;71(2):138–143. DOI: 10.1159/000076674.
32. Hahn-Pedersen J, Boxall N, Maier W, et al. Systematic literature review assessing data on the burden of allergic rhinitis from a cost and quality of life perspective. Value Health 2014;17:602. DOI: 10.1016/j.jval.2014.08.2087.
33. Lofaso F, Coste A, d'Ortho MP, et al. Nasal obstruction as a risk factor for sleep apnoea syndrome. Eur Respir J 2000;16(4):639–643. DOI: 10.1034/j.1399-3003.2000.16d12.x.
34. Calais CJ, Robertson BD, Beakes DE. Association of allergy/immunology and obstructive sleep apnea. Allergy Asthma Proc 2016;37(6):443–449. DOI: 10.2500/aap.2016.37.4001.
35. Aurora RN, Collop NA, Jacobowitz O, et al. Quality measures for the care of adult patients with obstructive sleep apnea. J Clin Sleep Med 2015;11(3):357–383. DOI: 10.5664/jcsm.4556.
36. Young T, Finn L, Kim H. Nasal obstruction as a risk factor for sleep-disordered breathing. The University of Wisconsin Sleep and Respiratory Research Group. J Allergy Clin Immunol 1997;99(2):757–762. DOI: 10.1016/s0091-6749(97)70124-6.
37. Chirakalwasan N, Ruxrungtham K. The linkage of allergic rhinitis and obstructive sleep apnea. Asian Pac J Allergy Immunol 2014;32(4):276–286. PMID: 25543037.
38. Kramer M, De La Chaux R, Dreher A, et al. Allergic rhinitis does not constitute a risk factor for obstructive sleep apnea syndrome. Acta Otolaryngol 2001;121(4):494–499. PMID: 11508511.
39. Gadi G, Albar M, Fida A, et al. The frequency of allergic rhinitis among obstructive sleep apnea patients: a hospital-based, cross-sectional study. JKAU Med Sci 2014;21(3):61–74. DOI: 10.4197/Med.21-3.5.
40. Duchna H, Rasche K, Lambers N, et al. Incidence of cutaneous sensitization to environmental allergens in obstructive sleep apnea syndrome. Pneumologie 1997;51(Suppl. 3):763–766. PMID: 9340635.
41. Bozkurt B, Serife Ugur K, Karamanli H, et al. Polysomnographic findings in persistent allergic rhinitis. Sleep Breath 2017;21(2):255–261. DOI: 10.1007/s11325-016-1390-4.
42. Buske-Kirschbaum A, Geiben A, Höllig H, et al. Altered responsiveness of the hypothalamus-pituitary-adrenal axis and the sympathetic adrenomedullary system to stress in patients with atopic dermatitis. J Clin Endocrinal Metab 2002;87(9):4245–4251. DOI: 10.1210/jc.2001-010872.

43. Bengtsson C, Jonsson L, Holmstrom M, et al. Impact of nasal obstruction on sleep quality: a community-based study of women. Eur Arch Otorhinolaryngol 2015;272(1):97–103. DOI: 10.1007/s00405-014-3067-6.
44. Gouder C, Fsadni P, Vella C, et al. Association between obstructive sleep apnea and atopy in adult Maltese patients. Ann Allergy Asthma Immunol 2016;117(4):441–442. DOI: 10.1016/j.anai.2016.07.040.
45. Cisternas A, Aguilar F, Montserrat JM, et al. Effects of CPAP in patients with obstructive apnoea: is the presence of allergic rhinitis relevant? Sleep Breath 2017;10(4):893–900. DOI: 10.1007/s11325-017-1510-9.
46. Berson SR, Klimczak J, Prezio EA, et al. Clinical associations between allergies and rapid eye movement sleep disturbances. Int Forum Allergy Rhinol 2018;8(7):817–824. DOI: 10.1002/alr.22099.
47. Pahus L, Gouitaa M, Sofalvi T, et al. Cypress pollen allergy is responsible for two distinct phenotypes of allergic rhinitis different from other pollinosis. Eur Ann Allergy Clin Immunol 2018;50(1):28–35. DOI: 10.23822/EurAnnACI.1764-1489.34.
48. Sibbald B, Barnes G, Durham SR. Skin prick testing in general practice: a pilot study. J Adv Nurs 1997;26(3):537–542. DOI: 10.1046/j.1365-2648.1997.t01-14-00999.x.
49. Burbach GJ, Heinzerling LM, Edenharter G, et al. GA(2)LEN skin test study II: clinical relevance of inhalant allergen sensitizations in Europe. Allergy 2009;64(10):1507–1515. DOI: 10.1111/j.1398-9995.2009.02089.x.
50. Bousquet J, Heinzerling L, Bachert C, et al. Practical guide to skin prick tests in allergy to aeroallergens. Allergy 2012;67(1):18–24. DOI: 10.1111/j.1398-9995.2011.02728.x.
51. Heinzerling L, Mari A, Bergmann KC, et al. The skin prick test—European standards. Clin Transl Allergy 2013;3(1):3. DOI: 10.1186/2045-7022-3-3.
52. American Academy of Sleep Medicine. International classification of sleep disorders: diagnostic and coding manual. 2nd ed. Westchester, IL: American Academy of Sleep Medicine; 2005.
53. Kapur VK, Auckley DH, Chowdhuri S, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine Clinical Practice Guideline. J Clin Sleep Med 2017;13(3):479–504. DOI: 10.5664/jcsm.6506.
54. Valovirta E, Myrseth SE, Palkonen S. The voice of the patients: allergic rhinitis is not a trivial disease. Curr Opin Allergy Clin Immunol 2008;8(1):1–9. DOI: 10.1097/ACI.0b013e3282f3f42f.
55. Calderón MA, Linneberg A, Kleine-Tebbe J, et al. Respiratory allergy caused by house dust mites: what do we really know? J Allergy Clin Immunol 2015;136(1):38–48. DOI: 10.1016/j.jaci.2014.10.012.
56. Calderón MA, Kleine-Tebbe J, Linneberg A, et al. House dust mite respiratory allergy: an overview of current therapeutic strategies. J Allergy Clin Immunol Pract 2015;3(6):843–855. DOI: 10.1016/j.jaip.2015.06.019.
57. Valletta, Malta Travel Weather Averages. Available from: weatherbase.com [Last accessed May 26, 2021].
58. Bodtger U. Prognostic value of asymptomatic skin sensitization to aeroallergens. Curr Opin Allergy Clin Immunol 2004;4(1):5–10. DOI: 10.1097/00130832-200402000-00003.
59. Santos CB, Pratt EL, Hanks C, et al. Allergic rhinitis and its effect on sleep, fatigue, and daytime somnolence. Ann Allergy Asthma Immunol 2006;97(5):579–671. DOI: 10.1016/S1081-1206(10)61084-8.
60. Kalpaklıoğlu AF, Kavut A, Ekici M. Allergic and nonallergic rhinitis: the threat for obstructive sleep apnea. Ann Allergy Asthma Immunol 2009;103(1):20–25. DOI: 10.1016/S1081-1206(10)60138-X.