The Symptoms and Signs of Upper Airway Resistance Syndrome*

A Link to the Functional Somatic Syndromes

Avram R. Gold, MD; Francis Dipalo, DO; Morris S. Gold, DSc; and Daniel O'Hearn, MD

Study objectives: The functional somatic syndromes are associated with a variety of symptoms/signs of uncertain etiology. We determined the prevalence of several of those symptoms/signs in patients with sleep-disordered breathing and examined the relationship between the prevalence of the symptoms/signs and the severity of sleep-disordered breathing.

Design: A descriptive study without intervention.

Setting: A university sleep-disorders center located in a suburban setting.

Patients or participants: Three groups of 25 consecutively collected patients with sleep-disordered breathing. Groups varied in their apnea hypopnea indexes (AHIs) as follows: upper airway resistance syndrome (UARS) [AHI < 10/h), mild-to-moderate obstructive sleep apnea/hypopnea (OSA/H) [AHI ≥ 10 to < 40/h), and moderate-to-severe OSA/H (AHI ≥ 40/h).

Measurements and results: Patients underwent comprehensive medical histories, physical examinations, and full-night polysomnography. The diagnosis of UARS included quantitative measurement of inspiratory airflow and inspiratory effort with demonstration of inspiratory flow limitation. The percentage of women among the patients with sleep-disordered breathing (p = 0.001) and the prevalence of sleep-onset insomnia (p = 0.04), headaches (p = 0.01), irritable bowel syndrome (p = 0.01), and alpha-delta sleep (p = 0.01) was correlated with decreasing severity of AHI group.

Conclusions: We conclude that patients with UARS, mild-to-moderate OSA/H and moderate-to-severe OSA/H differ in their presenting symptoms/signs. The symptoms/signs of UARS closely resemble those of the functional somatic syndromes.   *(CHEST 2003; 123:87–95)*

Key words: alpha-delta sleep; bruxism; chronic fatigue syndrome; fibromyalgia; functional somatic syndromes; irritable bowel syndrome; sleep-disordered breathing; temporomandibular joint syndrome; upper airway resistance syndrome

Abbreviations: AHI = apnea/hypopnea index; BMI = body mass index; CMH = Cochran-Mantel-Haenszel; CPAP = continuous positive airway pressure; IBS = irritable bowel syndrome; NREM = non-rapid eye movement; OSA/H = obstructive sleep apnea/hypopnea; Pmask = nasal mask pressure; UARS = upper airway resistance syndrome

During the past decade, physicians treating sleep disorders have experienced a broadening of the spectrum of sleep-disordered breathing. In addition, to the obstructive sleep apnea/hypopnea syndrome (OSA/H), many researchers and clinicians now recognize the upper airway resistance syndrome (UARS).[1] Both OSA/H and UARS often present with the signs/symptoms of snoring, fitful sleep, and daytime sleepiness/fatigue. The chief difference between the two syndromes can be found in the airflow

---

For editorial comment see page 12

---

channel of the polysomnogram. While patients with both syndromes experience recurrent arousals from sleep, OSA/H patients demonstrate decreases of inspiratory flow to < 50% of waking levels associated with oxyhemoglobin desaturation, while patients with UARS have less severe inspiratory flow limitation.[1,2] In a previous study,[2] we demonstrated that the less severe inspiratory flow limitation of patients with UARS during sleep is associated with a less collapsible upper airway.

When viewed from the perspective of upper airway physiology, patients with UARS and patients with OSA/H are similar, differing only in the severity of their upper airway collapsibility during sleep. In a recent editorial, however, Guilleminault and Chowdhuri[3] suggested that patients with UARS are younger and more often female than patients with OSA/H and complain more frequently of sleep-onset insomnia and fatigue. In addition, Guilleminault and associates[4] found a greater prevalence of orthostatic intolerance in patients with UARS than in patients with OSA/H. In our previous study,[2] we observed similar age and gender differences between patients with UARS and patients with OSA/H. Furthermore, it has been our impression that patients with UARS whom we see in our practice present with sleep-onset insomnia, headaches, gastroesophageal reflux, depression, bruxism (grinding of teeth), symptoms of rhinitis, hypothyroidism, and asthma more frequently than do patients with OSA/H. These observations have led us to hypothesize that patients with UARS have a different clinical presentation from patients with OSA/H.

In addition to the differences we have observed between patients with UARS and patients with OSA/H in demographics and symptoms/signs, we have observed a remarkable feature in the polysomnograms of several of our patients with UARS: the EEG finding of alpha-delta sleep.[5] Alpha-delta sleep, the intrusion of waking alpha rhythm into deep, slow-wave sleep, is not known to be a feature in patients with OSA/H. Rather, it has been observed in a variety of syndromes associated with chronic fatigue.[6–8] The functional somatic syndromes[9–11] include chronic fatigue syndrome,[12] fibromyalgia,[13] irritable bowel syndrome (IBS),[14,15] migraine/tension headaches,[16] and temporomandibular joint syndrome.[7,17,18] In addition to a common symptom of excessive sleepiness/fatigue, these syndromes feature the following symptoms/signs: sleep-onset and maintenance insomnia, unrefreshing sleep, EEG evidence of sleep fragmentation, bruxism, muscle pain and tenderness, heartburn, abdominal pain/urgency, diarrhea, headaches, depression, and orthostatic syncope.[19,20] Thus, the symptoms/signs we have observed in patients with UARS appear to overlap substantially with the symptoms/signs of the functional somatic syndromes.

Combining the findings of previous investigators and our observations above, we hypothesized that patients with UARS have a clinical presentation that differs from that of patients with OSA/H and resembles the clinical presentation of the functional somatic syndromes. To test this hypothesis, we have determined the prevalence of a variety of symptoms/signs in consecutively evaluated patients with sleep-disordered breathing.

MATERIALS AND METHODS

The study is a prospective examination of the prevalence of a variety of symptoms/signs in 75 patients with UARS and OSA/H (25 consecutive patients with sleep-disordered breathing at each of three levels of severity). All of the patients were referred to the SUNY Sleep Disorders Center–Medicine because of a clinical suspicion of sleep-disordered breathing. Patients with fibromyalgia referred for evaluation of sleep-disordered breathing[21] were excluded because they would be expected to have the symptoms of the functional somatic syndromes. This study was approved by the Institutional Review Board of SUNY at Stony Brook School of Medicine.

Evaluation of Sleep-Disordered Breathing

Consultation: On scheduling a sleep consultation, each patient received a detailed general medical history questionnaire and a sleep-related symptoms questionnaire to complete and bring to the consultation. The sleep consultation was performed by a physician with credentials in both internal medicine and sleep medicine, and included a general medical and sleep-related history and physical examination.

Full-Night Polysomnography: Polysomnography was performed between the hours of 10 PM and 6 AM. Sleep stages were monitored using surface EEG activity of the central and occipital regions, submental surface electromyographic activity, and left and right electro-oculographic activity. Leg movement was detected using surface electromyographic activity of the right and left tibialis anterior muscle. Airflow at the nose and mouth was monitored with a thermocouple. Thoracoabdominal movement was monitored with piezoelectric belts. Oxyhemoglobin saturation was monitored at the finger using a pulse oximeter. A continuous ECG monitored heart rate and rhythm. All of the data were converted from analog to digital and stored on a computer for analysis by a board-certified sleep physician.

Respiratory events were defined as any combination of apnea and hypopnea lasting at least 10 s and associated with an arousal. Apnea was defined as a decrease of inspiratory airflow to < 20% of waking levels, and hypopnea was defined as a decrease in inspiratory airflow to < 50% of waking levels. The clinical diagnosis of OSA/H was established by an apnea/hypopnea index (AHI) of at least 10 events per hour of sleep. Patients presenting with symptoms of sleep-disordered breathing, but with an AHI of < 10/h received a presumptive diagnosis of UARS. The diagnosis of UARS was confirmed after further evaluation with a diagnostic nasal continuous positive airway pressure (CPAP) study.

Nasal CPAP Study: All patients with a presumptive diagnosis of UARS underwent a nasal CPAP study to demonstrate inspiratory airflow limitation during non-rapid eye movement (NREM) sleep (confirming UARS) and to determine a therapeutic level of nasal CPAP.

During the nasal CPAP study, each patient slept wearing a nasal CPAP mask (Respironics; Murrysville, PA). The mask was attached via a breathing circuit and a bi-directional valve to a source of CPAP and to a source of negative pressure (a modified Rem-Star unit; Respironics). Using the dual pressure sources, we were able to vary the mask pressure between − 20 cm H_2O and 20 cm H_2O. The monitoring of sleep stages, leg movements, heart rhythm, and oxyhemoglobin saturation during the nasal CPAP study was the same as for polysomnography. Nasal airflow

was measured with a heated pneumotachograph (model 3813; Hans Rudolph; Kansas City, MO) and transducer (model MP45–14-871 S/N 45534; Validyne Engineering; Northridge, CA) interposed between the bi-directional valve and the nasal mask. Inspiratory effort was measured as esophageal pressure using a saline solution-filled infant feeding tube with side ports at its distal 1 cm attached to a disposable pressure transducer (model 00-041576504A; Maxxim; Athens, TX). The distal 1 cm of the feeding tube was positioned in the middle third of the esophagus. Nasal mask pressure (Pmask) was monitored directly from a port in the mask using a differential pressure transducer (model 231D; Spectramed; Oxnard, CA) referenced to atmosphere.

Our methods for evaluating upper airway pressure/flow relationships have been described previously.[2] To demonstrate sleep-related inspiratory flow limitation, Pmask is set at atmospheric pressure (between 1 cm H_2O and − 1 cm H_2O). Inspiratory flow limitation is considered to occur when inspiratory airflow becomes maximal despite an increasing driving pressure for airflow (a decreasing esophageal pressure).

Because our laboratory does not place an esophageal catheter for every clinical polysomnogram, we cannot establish the diagnosis of UARS by demonstrating respiratory effort-related arousals during full-night polysomnography.[22] In our laboratory, the combination of excessive daytime sleepiness/fatigue, an AHI < 10/h, and evidence of inspiratory flow limitation during NREM sleep with Pmask at atmospheric pressure establishes the diagnosis of UARS.

Symptoms and Signs: We chose and defined the following symptoms/signs to investigate:

1. Sleep-onset insomnia: a subjective inability to fall asleep in < 30 min.
2. Headaches: a diagnosis of migraine headaches established by a physician or the occurrence of any headache (other than a morning headache on awakening) at least once weekly.
3. Rhinitis: any two of the following: the chronic presence of nasal stuffiness, the chronic presence of postnasal drip, chronic or seasonal nasal allergies.
4. Gastroesophageal reflux: a diagnosis of gastroesophageal reflux established by a physician or the presence of heartburn (every week) for which the patient regularly receives antacids or histamine type-2 blocking agents.
5. Asthma: a diagnosis of asthma established by a physician or the presence of wheezing during our physical examination of a nonsmoker.
6. Depression: The diagnosis of depression by a psychiatrist or psychologist, or the diagnosis by an internist associated with the prescription of antidepressant medication.
7. Hypothyroidism: diagnosed by a physician and treated with thyroid replacement.
8. Bruxism: the observation by a bed partner of "tooth grinding" or the observation by a dentist of the characteristic tooth wear.
9. Alpha-delta sleep: a polysomnographic EEG pattern characterized by the superimposition of alpha rhythm on the delta rhythm of slow-wave sleep (Fig 1). The presence of alpha-delta sleep was determined by a board-certified sleep physician evaluating the full-night polysomnogram (first sleep study).
10. IBS: a diagnosis of IBS established by a physician or the regular occurrence of two of the following symptoms: diarrhea alternating with constipation, abdominal pain/urgency, or gaseous bloating.
11. Orthostatic syncope: the frequent experiencing of "light headedness" (not a sensation of "spinning") on arising from a seated or supine position in a patient not being treated with diuretics or antihypertensives.

We chose the first nine symptoms/signs because our clinical experience suggested that their prevalence would be greater in patients with UARS than in patients with OSA/H. We included the last two symptoms/signs because they have been observed in the functional somatic syndromes. We had not previously screened our patients with sleep-disordered breathing for symptoms of either IBS or orthostatic syncope. Only current symptoms/signs were considered present. Symptoms/signs that had been experienced prior to our consultation, but that did not continue, were considered absent.

Experimental Design: To ensure a broad range of sleep-disordered breathing severity in our patients, we collected 25 consecutive patients at each of three levels of severity of AHI: UARS (AHI < 10/h), mild-to-moderate OSA/H (AHI ≥ 10 to < 40/h), and moderate-to-severe OSA/H (AHI ≥ 40/h). We reviewed each patient's questionnaires, history, physical examination, and polysomnogram to abstract the needed information. Whenever our review determined that information was missing, the physician who performed the consultation obtained the missing information during the next clinical contact (usually within 1 month of polysomnography). The designation of symptoms/signs as "present" or "absent" according to the criteria listed above was done by individuals blinded to the severity of the patient's sleep-disordered breathing.
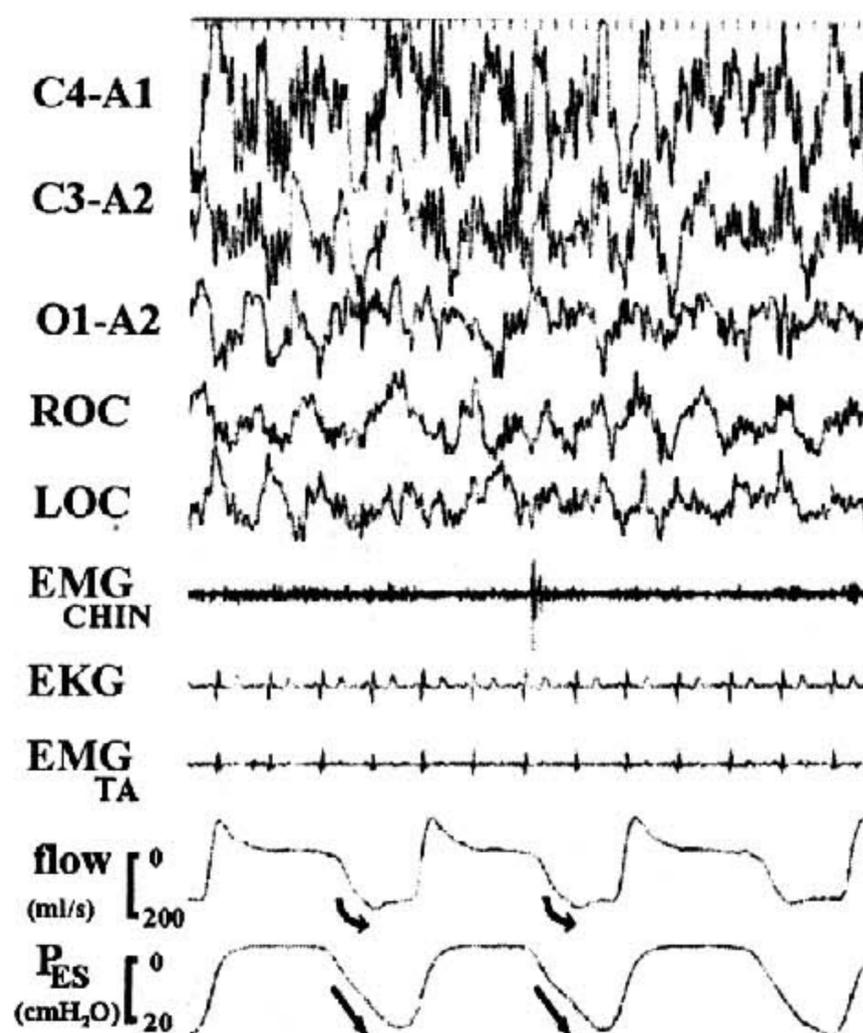

FIGURE 1. Alpha-delta sleep in a 53-year-old woman with snoring, severe sleepiness, an AHI of 0/h, and an arousal frequency of 29/h. The central EEG channels (C4-A1 and C3-A2) demonstrate low-frequency (< 2 cycles per second), high-amplitude (> 75 μV) delta waves with superimposed 7 to 11 cycle per second α waves characteristic of alpha-delta sleep. The airflow channel (flow) demonstrates a plateau of inspiratory airflow (downgoing; curved arrow) despite a continuing increase in the pressure driving airflow, the decreasing intrathoracic pressure (Pes; downgoing arrow), characterizing inspiratory flow limitation. ROC/LOC are right and left electro-oculograms; EMGchin/EMGta are surface electromyograms of the chin and tibialis anterior muscle, respectively.

RESULTS

The anthropometric and AHI data of our three groups of patients with sleep-disordered breathing are shown in Table 1. The patients with UARS were significantly younger than the patients with mild-to-moderate OSA/H (p = 0.036), but were not significantly younger than the patients with moderate-to-severe OSA/H. The patients with UARS had a significantly lower body mass index (BMI) than either group of patients with OSA/H (p < 0.02 for each comparison). Female patients constituted a significantly larger portion of the UARS group than of either OSA/H group (p < 0.02 for each comparison), with the prevalence of women among the patients progressively decreasing as the severity of AHI group increased (p = 0.0005, CMH test of zero correlation).

The sleep-related symptoms of our 75 patients are shown in Table 2. Nearly all of our patients had complaints of both sleepiness/fatigue and snoring. The three patients with UARS who did not have a history of snoring presented with sleepiness/fatigue and fitful, restless sleep. The two patients with mild-to-moderate OSA/H who did not complain of sleepiness/fatigue both had histories of snoring and witnessed apnea.

The relationship between the decreasing severity of AHI group and the prevalence of symptoms/signs of sleep-disordered breathing is demonstrated in Figure 2. There was a significant correlation between decreasing severity of AHI group and the

Table 1—*Anthropometric and AHI Data**

Variables	UARS	Mild-to-Moderate OSA/H	Moderate-to-Severe OSA/H
Age, yr	43 (15)†	52 (13)	48 (14)
BMI	29.9 (6)‡	35.6 (9)	38.4 (8)
Male/female gender	13/12†	5/20	2/23
AHI, events/h	1.5 (2.3)	25.1 (10.2)	68.8 (17.4)

*Data are presented as mean (SD) or No.
†p = 0.036 vs mild-to-moderate OSA/H group.
‡p < 0.02 vs both OSA/H groups.

Table 2—*Sleep-Related Symptoms**

Variables	UARS	Mild-to-Moderate OSA/H	Moderate-to-Severe OSA/H
Sleepiness/ fatigue	25 (100)	23 (92)	25 (100)
Snoring	22 (88)	25 (100)	25 (100)
Witnessed apnea	9 (36)	16 (64)	21 (84)
Fitful, restless sleep	16 (64)	17 (68)	16 (64)

*Data are presented as No. (% of group).

prevalence of sleep-onset insomnia (p = 0.04), headache (p = 0.01), IBS (p = 0.01), and alpha-delta sleep (p = 0.01). Nonsignificant trends were present for the prevalence of bruxism (p = 0.16) and rhinitis (p = 0.16). Unlike the symptoms/signs that increased in prevalence with decreasing severity of AHI, the prevalence of rhinitis tended to decrease as severity of AHI decreased. There was no significant correlation between the prevalence of depression, GERD, asthma, hypothyroidism, or orthostatic syncope and the severity of AHI.

Alpha-delta sleep was present in six of our patients with UARS ($8.9 \pm 8.5\%$ of total sleep time), in three of our patients with mild-to-moderate OSA/H ($13.7 \pm 7.4\%$ of total sleep time), and in none of our patients with moderate-to-severe OSA/H. In patients with alpha-delta sleep, the finding was present in all slow-wave sleep observed during polysomnography. Furthermore, each patient with alpha-delta sleep during full-night polysomnography also had the finding during the CPAP study. Each patient without alpha-delta sleep during polysomnography did not display alpha-delta sleep during the CPAP study.

To evaluate whether the symptoms/signs whose prevalence were greatest in patients with UARS were widely distributed among those patients, or whether they were clustered in a small group of patients with numerous symptoms/signs, we chose five symptoms/signs that tended to be most prevalent in patients with UARS (sleep-onset insomnia, headache, IBS, alpha-delta sleep, and bruxism) and counted the frequency of these symptoms/signs in each patient with sleep-disordered breathing (Fig 3). We found that the five symptoms/signs tended to be widely distributed among patients with UARS. More than 96% of the patients with UARS had at least one symptom/sign, with 72% having from two to four symptoms/signs, Despite their decreased prevalence, the symptoms/signs were also widely distributed among patients with OSA/H, with 64% having at least one symptom/sign. Thus, the symptoms/signs that tended to be more prevalent in patients with UARS were broadly distributed among
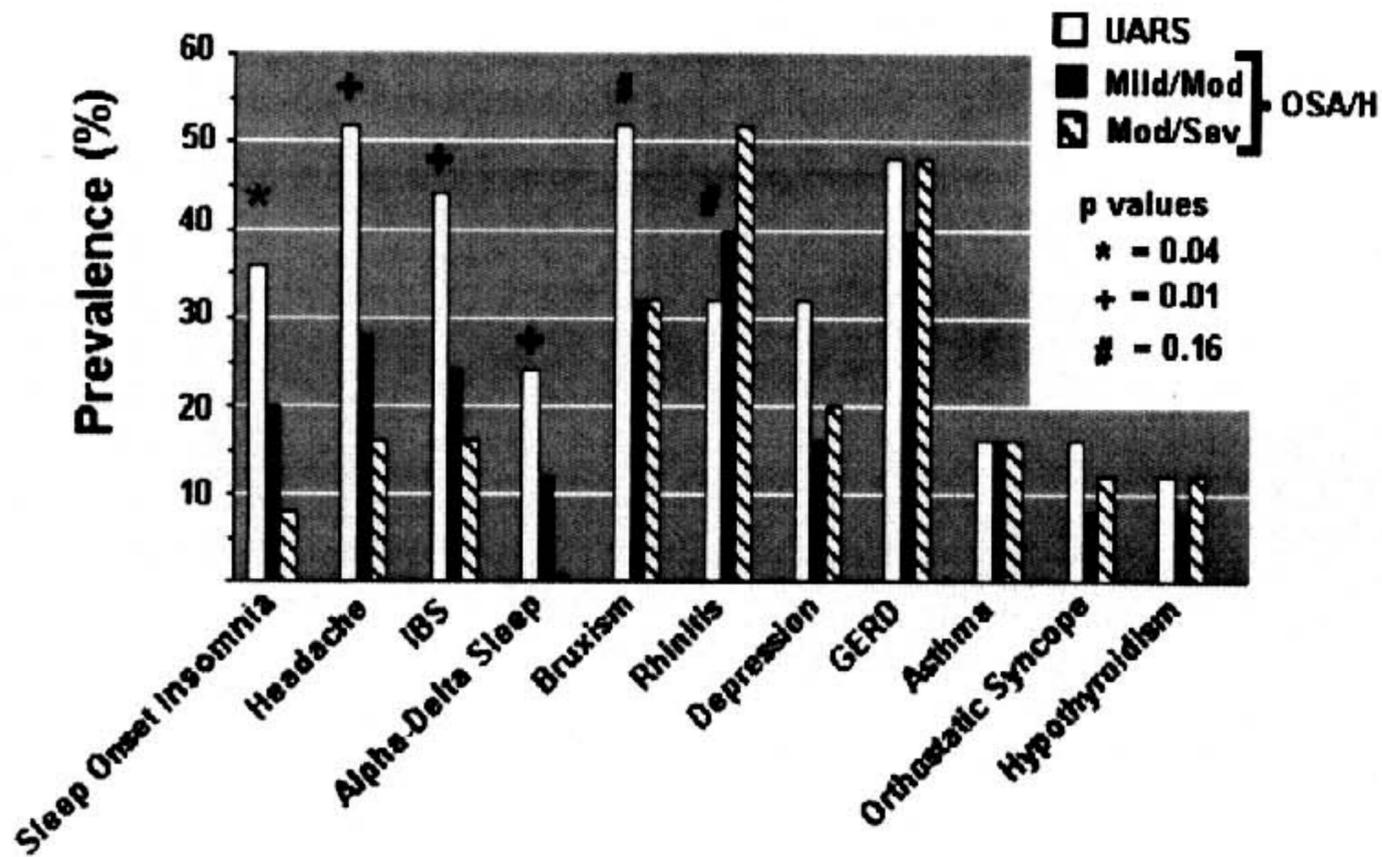
FIGURE 2. Prevalence of the various symptoms/signs in our patients with sleep-disordered breathing. The prevalence of sleep-onset insomnia, headache, IBS, and alpha-delta sleep increased with decreasing severity of AHI group to a statistically significant degree. Mod = moderate; Sev = severe.

patients with sleep-disordered breathing and not just clustered in a small subset of patients with numerous symptoms/signs.

Because the functional somatic syndromes have a predilection for female subjects,[11] and the percentage of women among our patients with sleep-disordered breathing increased with decreasing severity of AHI group, it could be argued that the differences observed in the prevalence of symptoms/signs between severity of AHI groups may have resulted from the gender differences between groups.[23] To investigate whether the increased prev-
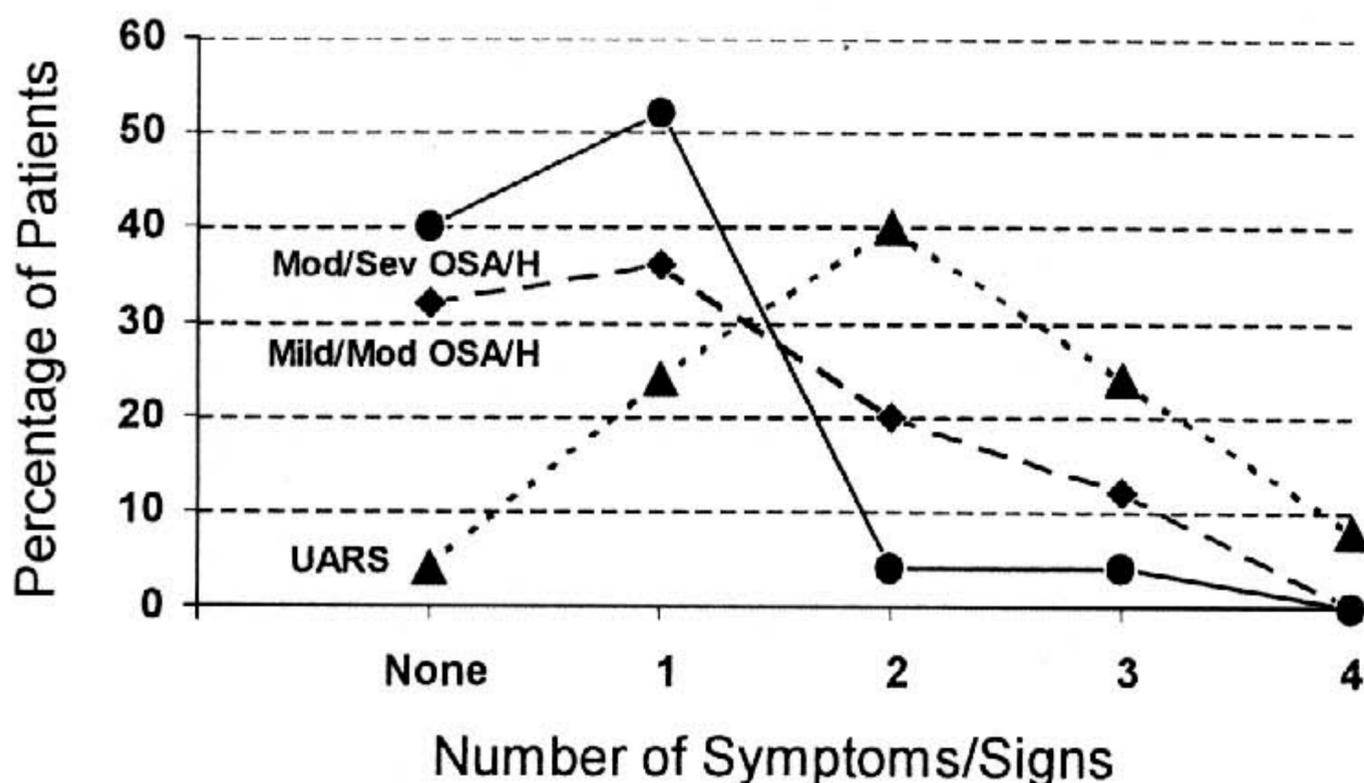
FIGURE 3. For the five symptoms/signs whose prevalence was greatest among UARS patients (sleep-onset insomnia, headache, IBS, alpha-delta sleep, and bruxism), this graph illustrates the clustering of those symptoms in individual patients. The signs and symptoms were widely distributed among patients with UARS (dotted line with triangles), patients with mild-to-moderate OSA/H (dashed line with diamonds), and patients with moderate-to-severe OSA/H (solid line with circles). See Figure 2 for expansion of abbreviations.

alence of women among our patients with UARS accounted for the significantly higher prevalence of some symptoms/signs in the same group, we examined the prevalence of those symptoms/signs in our patients with sleep-disordered breathing as a function of gender using the CMH test of zero correlation controlled for gender (Table 3). We found that the significant correlation between decreasing severity of AHI group and the prevalence of sleep-onset insomnia, headache, and alpha-delta sleep in Figure 2 remained apparent. The correlation became weakened for IBS (p value increased from 0.01 to 0.10; IBS was common in women with OSA/H), but was greatly strengthened for bruxism (p value decreased from 0.16 to 0.05). On the whole, the impression from Table 3 is that the prevalence of the indicated symptoms/signs increases as severity of AHI decreases.

DISCUSSION

In this series of patients with sleep-disordered breathing, we have investigated the relationship between the severity of sleep-disordered breathing and the prevalence of a variety of symptoms/signs, many of which are associated with functional somatic syndromes. We have found that the percentage of women and the prevalence of sleep-onset insomnia, headache, IBS, and alpha-delta sleep are high among patients with UARS and decrease progressively with increasing severity of sleep-disordered breathing. These symptoms/signs appear to be widely distributed among patients with sleep-disordered breathing rather than restricted to a particular subgroup. The prevalence differences in the various symptoms/signs remained largely intact when differences between the groups in gender distribution were accounted for. These findings confirm our impression that UARS differs from moderate-to-severe OSA/H in its symptoms/signs, and it shares common symptoms/signs with the functional somatic syndromes.

In our previous study of upper airway collapsibility in patients with UARS and OSA/H, we found that patients with UARS, mild-to-moderate OSA/H, and moderate-to-severe OSA/H represent a continuum of increasing upper airway collapsibility.[2] Our findings in this study suggest that the symptoms/signs of sleep-disordered breathing also constitute a continuum. At the extremes of sleep-disordered breathing severity (UARS vs moderate-to-severe OSA/H), we found clear differences in clinical features. Our UARS patients were 50% female, with a high prevalence of sleep-onset insomnia, headache, IBS, and alpha-delta sleep. In contrast, our patients with moderate-to-severe OSA/H were 8% female, with a lower prevalence of sleep-onset insomnia, headache, IBS, and alpha-delta sleep. Consistent with a continuous progression of symptom/sign prevalence, our patients with mild-to-moderate OSA/H were 20% female, with an intermediate prevalence of sleep-onset insomnia, headache, IBS, and alpha-delta sleep. These findings suggest that the physiologic continuum of upper airway collapsibility during sleep that characterizes sleep-disordered breathing is paralleled by a continuous progression of the prevalence of symptoms/signs. There does not appear to be a discrete UARS.

While it is evident that the prevalence of symptoms/signs among patients with sleep-disordered breathing of varying severity constitutes a continuous progression, the direction of that progression appears counterintuitive. In patients with the least severe sleep-disordered breathing (UARS), the prevalence of sleep-onset insomnia, headaches, IBS, and alpha-delta sleep is highest, while in patients with the most severe sleep-disordered breathing (moderate-to-severe OSA/H), the prevalence of the same symptoms is lowest. Why does the prevalence of sleep-onset insomnia, headache, IBS, and alpha-delta sleep decrease as the severity of sleep-disordered breathing increases? Although our data do not answer this question, they may provide a clue. The increased prevalence of alpha-

Table 3—*Relationship Between Gender and the Prevalence of Symptoms/Signs**

Variables	Sleep-Onset Insomnia		Headache		IBS		Alpha-Delta Sleep		Bruxism	
	F	M	F	M	F	M	F	M	F	M
UARS	23	50	53	50	53	33	23	25	38	67
Mild-to-moderate OSA/H		15		30		15		10		35
	28		14		43		14		14	
Moderate-to-severe OSA/H		10		17		17		0		35
	(p = 0.04)		(p = 0.01)		(p = 0.10)		(p = 0.02)		(p = 0.05)	

*Data are presented as %. Because only seven women had OSA/H, we did not subdivide women with OSA/H into AHI groups. p Values were obtained using the CMH test of zero correlation controlled for gender. F = female; M = male.

delta sleep in patients with UARS indicates that the quality of their sleep is different from that of patients with moderate-to-severe OSA/H. In patients with functional somatic syndromes, the marked intrusion of alpha rhythm into slow-wave sleep is known to be associated with alpha intrusion into other NREM sleep stages and a high frequency of subjective sleep complaints.[24] Therefore, alpha-delta sleep may represent a diminution in the quality of sleep of patients with UARS. The adulterated sleep of patients with UARS may explain their complaints of sleep-onset insomnia, and it may contribute to autonomic dysfunction manifested as headache and IBS. The reason for the increasing prevalence of alpha-delta sleep, sleep-onset insomnia, headache, and IBS with decreasing severity of AHI warrants further study.

While our study indicates a difference between the symptoms/signs of UARS and those of moderate-to-severe OSA/H, we have no data comparing the symptoms/signs of UARS with those of gender-matched outpatients without sleep-disordered breathing. Such a comparison is needed to know whether the symptoms/signs more prevalent in patients with UARS result from inspiratory flow limitation during sleep. It is possible that having moderate-to-severe OSA/H protects against having functional somatic syndrome symptoms/signs. The absence of the symptoms/signs in a gender-matched group of outpatients without sleep-disordered breathing would suggest that inspiratory flow limitation during sleep is needed for the development of functional somatic syndrome symptoms/signs. Unfortunately, finding a gender-matched sample of outpatients known to be without sleep-disordered breathing was beyond the scope of our study. Thus, we cannot be certain that the symptoms/signs associated with UARS are unique to patients with inspiratory airflow limitation during sleep.

The presence of alpha-delta sleep in several of our patients with UARS and the apparent comorbidity between UARS and the functional somatic syndromes led to our interest in examining the relationship between the severity of sleep-disordered breathing and the functional somatic syndrome symptoms/signs. Patients with functional somatic syndromes constitute a large group seen by internists specializing in rheumatology, infectious disease, and gastroenterology, and by mental health professionals. In the United Kingdom, it is estimated that functional somatic syndrome symptoms constitute 20 to 25% of the complaints of patients seen in outpatient internal medicine practices.[11] The functional somatic syndromes are a large group of disorders of uncertain etiology. Included among these syndromes are chronic fatigue syndrome, fibromyalgia, IBS, tem-

poromandibular joint syndrome, and migraine/tension headache syndrome. The syndromes affect female patients more commonly than male patients and tend to overlap, sharing many common symptoms/signs. Among these symptoms are fatigue, sleep-onset and maintenance insomnia,[7,13] unrefreshing sleep,[12,13] EEG anomalies during sleep,[5–8,24] body pain and tenderness,[12,13,16,18] heartburn, abdominal pain/urgency and diarrhea,[14,15] headaches,[7,12,16] and depression.[13,16] Treatment of the functional somatic syndromes is largely symptomatic and of limited efficacy, relying heavily on analgesics, psychotropic medication, physical therapy, and psychotherapy.[9,11] Thus, the symptoms/signs of patients with UARS are similar to those of a large group of patients with syndromes of uncertain etiology whose treatments are of limited efficacy.

The functional somatic syndromes are thought to be multiaxial syndromes in which psychological factors (depression), neurologic factors (increased pain sensitivity), hormonal factors (orthostatic hypotension and alterations in the hypothalamic-pituitary-adrenal axis), and sleep-related factors (frequent arousals and alpha frequency intrusion into sleep) interact to produce a complex clinical presentation.[25] By demonstrating that the symptoms/signs of UARS resemble those of the functional somatic syndromes, we have introduced the possibility that unrecognized inspiratory flow limitation during sleep plays a role in the development of functional somatic syndromes. Specifically, the frequent arousals and alpha wave intrusion into the sleep of patients with functional somatic syndromes and the nonrestorative sleep associated with these syndromes may result from inspiratory flow limitation. Determining if inspiratory flow limitation during sleep causes the sleep fragmentation of the functional somatic syndromes will require further study.

While the significance of finding the symptoms of functional somatic syndromes in patients with sleep-disordered breathing is uncertain, several studies have found a high prevalence of sleep-disordered breathing in samples of patients with functional somatic syndromes. Buchwald and associates[26] studied the sleep of patients with chronic fatigue syndrome and found that nearly half of these patients had OSA/H. Kumar and associates[27] studied the sleep of patients with IBS and observed OSA/H in three of six patients with IBS, but in none of six control subjects. In studies of the sleep of patients with fibromyalgia, investigators have demonstrated the presence of recurrent oxyhemoglobin desaturations,[28] periodic breathing,[29] and OSA/H.[21] All of the previous studies screened patients for OSA/H as the only manifestation of sleep-disordered breathing. Had

previous investigators screened patients for milder inspiratory airflow limitation, it is possible that they would have observed an even stronger association between sleep-disordered breathing and the functional somatic syndromes.

Although our study provides useful information concerning the clinical presentation of sleep-disordered breathing, our methods have a limitation. Specifically, we did not confirm each patient's medical history by obtaining the patient's medical record. We do not believe, however, that our study is greatly limited by this factor. Nearly all the patients utilizing our suburban, sleep-disorders center are sophisticated individuals with health insurance and primary care providers. Thus, our patients had ready access to evaluation of their health-related complaints and knowledge of their medical histories. Moreover, for subjective symptoms like sleep-onset insomnia, headache, and IBS, obtaining the medical record would provide little support for the patients' histories. Thus, we do not believe that our not obtaining the patients' medical records limits the conclusions that we can draw from this study.

The sample size of our study (75 patients) limited our capacity to control for covariance and limited the conclusions we can draw from our data. Although we were able to control for gender, we were not able to concomitantly control for BMI, which increased with increasing AHI group. It can be argued, however, that while it is necessary to control for gender differences (because gender is known to be correlated with the symptoms/signs of the functional somatic syndromes), it is not necessary to control for BMI. Differences in BMI have not been associated with the prevalence of functional somatic syndrome symptoms/signs. Nevertheless, our sample size does limit our capacity to be certain that the AHI (and not other factors) is responsible for the prevalence of the symptoms/signs of the functional somatic syndromes in patients with sleep-disordered breathing.

In conclusion, our findings suggest that the clinical presentation of UARS differs from that of moderate-to-severe OSA/H, while it resembles the clinical presentation of the functional somatic syndromes. Our findings, however, do not prove that the functional somatic syndromes are caused by inspiratory flow limitation during sleep. Rather, they raise many questions. How are upper airway collapse during sleep and symptoms/signs such as sleep-onset insomnia, headaches, IBS, and alpha-delta sleep related? How would treatment of sleep-disordered breathing affect concomitant symptoms/signs other than sleepiness/fatigue? Does unrecognized inspiratory airflow limitation play a role in the functional somatic syndromes? The answers to these questions may lead to improvements in the diagnosis and management of sleep-disordered breathing and the functional somatic syndromes.

REFERENCES

1 Guilleminault C, Stoohs R, Clark A, et al. A cause of excessive daytime sleepiness: the upper airway resistance syndrome. Chest 1993; 104:781–787

2 Gold A, Marcus C, Dipalo F, et al. Upper airway collapsibility during sleep in upper airway resistance syndrome. Chest 2002; 121:1531–1540

3 Guilleminault C, Chowdhuri S. Upper airway resistance syndrome is a distinct syndrome. Am J Respir Crit Care Med 2000; 161:1412–1413

4 Guilleminault C, Faul JL, Stoohs R. Sleep-disordered breathing and hypotension. Am J Respir Crit Care Med 2001; 164:1242–1247

5 Hauri P, Hawkins DR. Alpha-delta sleep. Electroencephalogr Clin Neurophysiol 1973; 34:233–237

6 Manu P, Lane TJ, Matthews DA, et al. Alpha-delta sleep in patients with a chief complaint of chronic fatigue. South Med J 1994; 87:465–470

7 Bader GG, Kampe T, Tagdae T, et al. Descriptive physiological data on a sleep bruxism population. Sleep 1997; 20:982–990

8 Moldofsky H, Scarisbrick P, England R, et al. Musculoskeletal symptoms and non-REM sleep disturbance in patients with "fibrositis syndrome" and healthy subjects. Psychosom Med 1975; 37:341–351

9 Barsky AJ, Borus JF. Functional somatic syndromes. Ann Intern Med 1999; 130:910–921

10 Aaron L, Buchwald D. A review of the evidence for overlap among unexplained clinical conditions. Ann Intern Med 2001; 134:868–881

11 Wessely S, Nimnuan C, Sharpe M. Functional somatic syndromes: one or many? Lancet 1999; 354:936–939

12 Fukuda K, Straus SE, Hickie I, et al. The chronic fatigue syndrome: a comprehensive approach to its definition and study; International Chronic Fatigue Syndrome Study Group. Ann Intern Med 1994; 121:953–959

13 Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia: report of the Multicenter Criteria Committee. Arthritis Rheum 1990; 33:160–172

14 Borum ML. Irritable bowel syndrome. Prim Care 2001; 28:523–538

15 Shen B, Soffer E. The challenge of irritable bowel syndrome: creating an alliance between patient and physician. Cleve Clin J Med 2001; 68:224–235

16 Dowson A, Jagger S. The UK migraine patient survey: quality of life and treatment. Curr Med Res Opin 1999; 15:241–253

17 Okeson JP, de Kanter RJ. Temporomandibular disorders in the medical practice. J Fam Pract 1996; 43:347–356

18 Plesh O, Wolfe F, Lane N. The relationship between fibromyalgia and temporomandibular disorders: prevalence and symptom severity. J Rheumatol 1996; 23:1948–1952

19 Bou-Holaigah I, Calkins H, Flynn JA, et al. Provocation of hypotension and pain during upright tilt table testing in adults with fibromyalgia. Clin Exp Rheumatol 1997; 15:239–246

20 Bou-Holaigah I, Rowe PC, Kan J, et al. The relationship between neurally mediated hypotension and the chronic fatigue syndrome. JAMA 1995; 274:961–967

21 May KP, West SG, Baker MR, et al. Sleep apnea in male patients with the fibromyalgia syndrome. Am J Med 1993; 94:505–508

22 American Academy of Sleep Medicine Task Force. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research: the report of an American Academy of Sleep Medicine task force. Sleep 1999; 22:667–689

23 Barsky AJ, Peekna HM, Borus JF. Somatic symptom reporting in women and men. J Gen Intern Med 2001; 16:266–275

24 Branco J, Atalaia A, Paiva T. Sleep cycles and alpha-delta sleep in fibromyalgia syndrome. J Rheumatol 1994; 21:1113–1117

25 Goldenberg DL. Fibromyalgia syndrome a decade later: what have we learned? Arch Intern Med 1999; 159:777–785

26 Buchwald D, Pascualy R, Bombardier C, et al. Sleep disorders in patients with chronic fatigue. Clin Infect Dis 1994; 18(Suppl 1):S68–S72

27 Kumar D, Thompson PD, Wingate DL, et al. Abnormal REM sleep in the irritable bowel syndrome. Gastroenterology 1992; 103:12–17

28 Lario BA, Baldivielso JLA, Lopez JA, et al. Fibromyalgia syndrome: overnight falls in arterial oxygen saturation. Am J Med 1996; 101:54–60

29 Sergi M, Rizzi M, Braghiroli A, et al. Periodic breathing during sleep in patients affected by fibromyalgia syndrome. Eur Respir J 1999; 14:203–208