ORIGINAL ARTICLE

Orofacial-cervical alterations in individuals with upper airway resistance syndrome∗

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Received 28 March 2015; accepted 29 May 2015
Available online 6 November 2015

KEYWORDS
Sleep disorders; Airway resistance; Nasal obstruction

Abstract
Introduction: Studies that assess the upper airways in sleep-related breathing disorders have been performed only in patients with obstructive sleep apnea syndrome who seek medical attention. Therefore, in addition to the need for population studies, there are no data on the orofacial-cervical physical examination in subjects with upper airway resistance syndrome.

Objectives: To compare the orofacial-cervical examination between volunteers with upper airway resistance syndrome and without sleep-related breathing disorders.

Methods: Through questionnaires, physical measurements, polysomnography, and otorhinolaryngological evaluation, this study compared the orofacial-cervical physical examination, through a systematic analysis of the facial skeleton, mouth, throat, and nose, between volunteers with upper airway resistance syndrome and volunteers without sleep-related breathing disorders in a representative sample of the adult population of the city of São Paulo.

Results: There were 1042 volunteers evaluated; 49 subjects (5%) were excluded as they did not undergo orotrinolaryngological evaluation, 381 (36%) had apnea-hypopnea index > 5 events/hour, and 131 (13%) had oxyhemoglobin saturation < 90%. Among the remaining 481 subjects (46%), 30 (3%) met the criteria for the upper airway resistance syndrome definition and 53 (5%) met the control group criteria. At the clinical evaluation of nasal symptoms, the upper

∗ Please cite this article as: de Oliveira PWB, Gregorio LL, Silva RS, Bittencourt LRA, Tufik S, Gregório LC. Orofacial-cervical alterations in individuals with upper airway resistance syndrome. Braz J Otorhinolaryngol. 2016;82:377-84.

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http://dx.doi.org/10.1016/j.bjorl.2015.05.015
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airway resistance syndrome group had more oropharyngeal dryness (17% vs. 29.6%; p = 0.025) and septal deviation grades 1–3 (49.1% vs. 57.7%; p = 0.025) when compared to controls. In the logistic regression model, it was found that individuals from the upper airway resistance syndrome group had 15.6-fold higher chance of having nose alterations, 11.2-fold higher chance of being hypertensive, and 7.6-fold higher chance of complaining of oropharyngeal dryness when compared to the control group.

Conclusion: Systematic evaluation of the facial skeleton, mouth, throat, and nose, between volunteers with upper airway resistance syndrome and volunteers without sleep-related breathing disorders, showed that the presence of upper airway resistance syndrome is mainly associated with nasal alterations and oropharyngeal dryness, in addition to the risk of hypertension, regardless of gender and obesity.

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**Introduction**

Upper airway resistance syndrome (UARS) was first described in 1982 in children and adults as “excessive daytime sleepiness.” At that time, such individuals were classified as having “idiopathic hypersonnia.” It was observed that a number of patients had polysonmographic characteristics in common, usually ignored in the sleep analysis at that time: progressive increase in respiratory effort (represented by esophageal pressure recording) culminating with a brief awakening, perceived through a change in the electroencephalogram (EEG) pattern. This respiratory event did not meet the criteria of apnea and/or hypopnea, but determined an excessive sleep fragmentation and, consequently, daytime sleepiness. Subsequently, it was suggested that an increase in upper airway (UA) resistance was responsible for these events, introducing the term UARS into the medical community.
Patients with obstructive sleep apnea syndrome (OSAS) have a high degree of collapsibility of the UA. Among several theories, it is believed that the entity may be explained by the dysfunction of the afferent receptors in pharynx. This dysfunction is not found in patients with UARS. Some authors have suggested that patients with UARS have small breathing difficulties, such as nasal valve collapse, inferior turbinate hypertrophy, and septal deviations. Moreover, it has been shown that changing the size of the UA during a respiratory event in patients with UARS produces a better and faster response, compared to patients with OSAS. Such response may be a reflex that leads to a subcortical activation, and is depicted in the electroencephalogram.

Patients with OSAS and UARS have similar complaints, such as fatigue and daytime sleepiness. However, patients with UARS do not meet the diagnostic criteria for OSAS, as they do not have a significant number of apneas and/or hypopneas (AHI < 5) associated with oxyhemoglobin desaturation. These patients have, during sleep, a high and increasing resistance to airflow during inhalation. This resistance is not enough to cause a significant change in the airflow as in OSAS, but it is enough to cause recurrent brief arousals that fragment sleep, leading to fatigue and daytime sleepiness. Despite the syndrome overlap, there are very important differences related to the frequency of insomnia, waking periods during the night, and difficulty falling asleep or returning to sleep, common complaints in patients with UARS.

Most studies assessing the UA in sleep-related breathing disorders (SRBD) are performed in patients with OSAS in a clinical population. There are no reports in the literature on the orofacial-cervical physical assessment in subjects with UARS. The objective of this study was to compare the orofacial-cervical physical assessment through a systematic evaluation of the facial skeleton, mouth, pharynx, and nose, between volunteers with UARS and volunteers without SRBD in a population sample representative of the city of São Paulo, in order to identify predictive characteristics of UARS.

**Methods**

A total of 1042 randomly selected subjects were included to represent the adult population of the city of São Paulo according to gender, age (20–80 years), and socioeconomic status. This sampling was based on the updated data of the population, according to estimates of Fundação SEADE, based on the 2000 census. The protocol was part of the larger project carried out in 2007, and was approved by the research ethics committee of the university (CEP 0591/09) and registered at ClinicalTrials.gov (NCT00596713).

All statistical procedures were performed using SPSS v. 17.0. The chi-squared test ($\chi^2$) with bimodal distribution was used as a measure of association to compare the frequencies between the groups. A logistic regression model using the backward Wald method for insertion of variables in the model was also used to identify the main predictors of UARS. A significance value of $P \leq 0.05$ was used for the interpretation of results.

**Standards for staging**

Sleep was staged according to the criteria proposed by Rechtschaffen and Kales. The arousals and periodic leg movements were staged according to the criteria proposed by the American Academy of Sleep Medicine in 2007. Respiratory events were analyzed according to the following definitions:

- Apneas (recommended rule): reduction $\geq 90\%$ in the amplitude of nasal airflow, lasting $\geq 10$ s.
- Hypopneas (alternative rule): reduction $\geq 50\%$ in the amplitude, lasting $\geq 10$ s, associated with a decrease in $\text{SpO}_2 \geq 3\%$ and/or waking episode at the EEG.
- Airflow limitation: ratio between the total time of airflow limitation by total sleep time, expressed as a percentage.

Subjects whose ratio was below the median of all assessed volunteers were considered as having airflow limitation at the polysomnography.

The orthonhinalaryngological assessment was performed by six previously trained orthonhinalaryngologists who were familiar with the routine of this examination, immediately prior to polysomnography preparation. Nasal complaints, physical examination of the UA, and facial skeleton were assessed. The investigation of nasal complaints addressed: nasal obstruction, nasal and/or oropharyngeal dryness, oral breathing, and use of oral or topical decongestants at that moment. Complaints were considered present when they occurred every day or almost every day.

The physical examination consisted of systematic inspection of the face, nasal endoscopy, and rhinoscopy. The body mass index (BMI) of individuals was also calculated using the formula: weight (kg)/height$^2$ (m$^2$), in addition to measures of neck circumference (measuring tape placed over the cricothyroid membrane and measured in cm). Nutritional status was classified as follows: normal weight (BMI $< 25$ kg/m$^2$), overweight (BMI $\geq 25$ kg/m$^2$ and $< 30$ kg/m$^2$), and obese (BMI $\geq 30$ kg/m$^2$).

The neck circumference was considered altered when $> 43$ cm in men or $> 38$ cm in women.

The evaluation of the facial skeleton, performed by inspection, was conducted by creating a virtual line passing by the outer edge of the lower lip perpendicularly to the floor, straight down to the chin, with the individual seated in the Frankfort horizontal position. When the anterior chin prominence was at a distance $> 2$ mm backwards in relation to the drawn line, the subject was considered as having a suggestive sign of mandibular retrusion.

Regardless the bony structures of the oral cavity, the presence of ogival hard palate and type of dental occlusion was assessed. Angle’s class II dental occlusion corresponds to the presence of the retruded mandible in relation to the maxilla, suggestive retrusion. As for the soft tissues of the oral cavity and oropharynx, the volume of the tongue, soft palate and uvula, tonsil size, and the modified Mallampati index were assessed. The tongue was considered large when it was marked by teeth, suggesting an alteration between content (tongue) and continent (oral cavity).

The soft palate was considered retruded when it was near the back wall of the oropharynx; web palate, when it showed...
low insertion of the posterior tonsillar pillar in the uvula, and thick, when it showed the presence of edema. The tonsillar pillars were considered medialized when they were close to the oropharyngeal midline. The uvula was considered long when it was close to the base of the tongue and thick when it showed the presence of edema.

The modified Mallampati index was performed as proposed by Friedman et al.,\(^2\) with the patient in the sitting position, with maximal mouth opening, and the tongue relaxed and positioned within the oral cavity. The subjects were classified into four grades: grade I (it is possible to visualize the entire oropharynx, including the soft palate, the tonsillar pillars, the tonsils, and the tip of the uvula), grade II (it is possible to visualize the upper pole of the tonsils and the uvula), grade III (it is possible to visualize part of the soft palate and the uvula), and grade IV (only the hard palate and part of the soft palate can be visualized). The palatine tonsils\(^12,13\) were classified as: grade I (intravelar), grade II (extending beyond the anterior tonsillar pillar), grade III (extending up to three-quarters of the midline), grade IV (completely obstructing the oropharynx). For individuals submitted to tonsillectomy, the nomenclature used was A0. Grades I and II were considered as non-obstructive hypertrophic palatine tonsils, and grades III and IV as obstructive.

Rhinoscopy was used to evaluate the presence of possible nasal septal deviation (NSD) and inferior turbinate hypertrophy (ITH). NSD was classified as grade I (deviation does not touch the inferior turbinates), grade II (deviation touches the inferior turbinates), or grade III (deviation touches the lateral wall, compressing the inferior turbinates). ITH was classified as present or absent. The nose was considered obstructed or “altered” in the presence of:

- Septal deviation grade II or III, or;
- Septal deviation grade I – nasal obstruction complaint or inferior turbinate hypertrophy, or;
- Inferior turbinate hypertrophy – nasal obstruction complaint.

The oropharynx was considered unfavorable\(^13,14\) when it had at least three of the following variables:

- Palatine tonsils grade III or IV
- Abnormal uvula (long and/or thick)
- Abnormal palate (posterior and/or thick)
- Web palate
- Medialized pillars.

The facial skeleton was considered unfavorable when it showed some of the following features: dental occlusion class II, retrognathia, ogival hard palate.

This UA assessment protocol in OSAS has been used and updated by the Department of Otorhinolaryngology and Head and Neck Surgery of the university where the present study was conducted for the writing of theses/dissertations, articles, resident training, classes for undergraduate students, courses, and conferences.

**Inclusion criteria for the group with UARS**

The volunteers that met the following criteria were included in the UARS group:

1. AHI < 5 events/hour.
2. Oxyhemoglobin saturation > 90% during sleep.
3. Awakening Index > 15 events/hour.
4. Airflow limitation > 6%.
5. Positive clinical picture: Epworth Sleepiness Scale (ESS) > 10 and/or fatigue scale > 4.

**Inclusion criteria for the control group**

The volunteers that met the following criteria were included in the control group:

1. AHI < 5 events/h.
2. Oxyhemoglobin saturation > 90% during sleep.
3. Awakening Index < 10 events/h.
4. Airflow limitation < 6%.
5. Negative clinical picture: ESS < 10 and/or fatigue scale < 4.

**Results**

During the EPISONO 2007 project, 1042 volunteers were assessed. A total of 49 subjects (5%) were excluded, as they did not undergo otorhinolaryngological assessment. Among the 993 subjects (95.30%) submitted to otorhinolaryngological assessment, 381 (38.6%) who had an AHI > 5 events/h were excluded, and 131 (13%) who had oxyhemoglobin saturation < 90% were excluded. Among the remaining 481 subjects (46%), 30 (3%) were assessed who met the criteria for UARS definition and 53 (5%) who met the control group criteria (Fig. 1).

Table 1 shows the comparison of anthropometric and sociodemographic characteristics of the control and UARS groups. Women accounted for 59% of the control group and 66.7% of the group with UARS (p < 0.46). The UARS group had fewer individuals aged 20–29 years (41.5% vs. 6.7%) and fewer aged between 60 and 80 years (3.8% vs. 13.3%).

There were no significant differences between the control group and UARS when habits and behaviors were assessed: consumption of caffeine, alcohol, smoking, illicit drug use, sleeping pills, and sedentary behavior (Table 2).

When the sleep symptoms were assessed, it was observed that the UARS group had more individuals with insomnia (complaints: 45.3% vs. 50%; DSM-IV: 5.7% vs. 23.3%), complaints of nocturnal awakening due to headache (3.8% vs. 30%), and fatigue and daytime sleepiness (ESS > 9: 0% vs. 53.3%). Table 3 shows a comparison of the systematic physical examination of the facial skeleton, nose, mouth, and pharynx performed in the control and UARS groups.

In the clinical evaluation of nasal symptoms, the UARS group had more oropharyngeal dryness (17% vs. 29.6%; p = 0.025) and septal deviation grades 1–3 (49.1% vs. 57.7%; p = 0.016). Although not statistically significant (p = 0.057), it was observed that the UARS group had a higher frequency of individuals with otorhinolaryngological nasal alterations (41.5% vs. 63%).
complaining of oropharyngeal dryness, when compared to the control group.

Discussion

This study compared sociodemographic characteristics, clinical symptoms related to sleep, and physical examination of volunteers with UARS and volunteers without SRBD in a population sample from São Paulo. Using a systematic assessment of the facial skeleton, nose, mouth, and pharynx, important, statistically significant differences were found between the two groups and regarding several variables, especially those related to the nose.

In the assessment of the nasal septal deviation, at the physical examination it was observed that individuals with UARS showed an increased frequency of some type of septal deviation when compared to the control group. When assessing the turbinate hypertrophy, a trend ($p = 0.08$) to a higher frequency of occurrence in the UARS group was observed when compared to the control group. It is known that septal deviations are not the only cause of nasal obstructions, but rather one of a number of alterations, such as inferior turbinate hypertrophy, nasal valve disorders, and others. For this reason, a variable to encompass these two variables together was created, termed “altered nose.”

The variable “altered nose,” which has been used in other studies, concomitantly assesses the three possible grades of septal deviation and its association with the inferior turbinates, whether or not hypertrophic, in order to determine whether the nose has airflow obstruction. This variable was created to differentiate a “normal” nose from a nose with significant alterations in nasal airflow during a typical assessment performed by an otorhinolaryngologist during a consultation. The main criticism of this variable is that this classification is a subjective assessment of nasal patency and may vary between different physicians. Acoustic rhinometry, however, provides an objective assessment of nasal patency, but it is not a commonly used method in clinical practice. During routine assessment, otorhinolaryngologists use the clinical complaint of nasal obstruction and the physical examination of the nose to help diagnose nasal obstruction, which are the same parameters used in this study.

During the assessment of the two groups, volunteers from the UARS group had a statistically increased frequency of “altered nose” when compared to the control group, i.e.,
Table 3  Frequency (%) of volunteers in the control and UARS groups, according to the systematic physical examination of the facial skeleton, nose, mouth, and pharynx.

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 53)</th>
<th>UARS (n = 30)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal obstruction</td>
<td>28.3</td>
<td>44.4</td>
<td>0.117</td>
</tr>
<tr>
<td>Oral breathing</td>
<td>28.3</td>
<td>38.5</td>
<td>0.255</td>
</tr>
<tr>
<td>Dryness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal</td>
<td>18.9</td>
<td>18.5</td>
<td></td>
</tr>
<tr>
<td>Oropharyngeal</td>
<td>17.0</td>
<td>29.6</td>
<td>0.025</td>
</tr>
<tr>
<td>Nasal septal deviation 1-3</td>
<td>49.1</td>
<td>76.9</td>
<td>0.016</td>
</tr>
<tr>
<td>Nasal septal deviation 2 and 3</td>
<td>17.0</td>
<td>30.8</td>
<td>0.134</td>
</tr>
<tr>
<td>Turbinate hypertrophy</td>
<td>38.5</td>
<td>57.7</td>
<td>0.086</td>
</tr>
<tr>
<td>Micrognathia</td>
<td>11.5</td>
<td>14.8</td>
<td>0.465</td>
</tr>
<tr>
<td>Ogival hard palate</td>
<td>28.3</td>
<td>22.2</td>
<td>0.381</td>
</tr>
<tr>
<td>Soft palate alterations (web, posterior, thick)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One type</td>
<td>45.3</td>
<td>37.0</td>
<td>0.194</td>
</tr>
<tr>
<td>Two types</td>
<td>15.1</td>
<td>33.3</td>
<td></td>
</tr>
<tr>
<td>Three types</td>
<td>5.7</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>Medialized pillars</td>
<td>17.0</td>
<td>3.7</td>
<td>0.085</td>
</tr>
<tr>
<td>Tonsil grade 2 and 3</td>
<td>18.9</td>
<td>14.8</td>
<td>0.453</td>
</tr>
<tr>
<td>Large tongue</td>
<td>22.6</td>
<td>26.9</td>
<td>0.439</td>
</tr>
<tr>
<td>Rhinopathy</td>
<td>54.7</td>
<td>51.9</td>
<td>0.497</td>
</tr>
<tr>
<td>Nasal treatment</td>
<td>5.8</td>
<td>14.8</td>
<td>0.176</td>
</tr>
<tr>
<td>Altered uvula</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long</td>
<td>9.4</td>
<td>11.1</td>
<td>0.564</td>
</tr>
<tr>
<td>Thick</td>
<td>5.7</td>
<td>14.8</td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>9.4</td>
<td>7.4</td>
<td></td>
</tr>
<tr>
<td>Mallampati 3 and 4</td>
<td>35.8</td>
<td>51.9</td>
<td>0.128</td>
</tr>
<tr>
<td>Otorhinolaryngological alterations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nose</td>
<td>41.5</td>
<td>63.0</td>
<td>0.057</td>
</tr>
<tr>
<td>Facial skeleton</td>
<td>7.5</td>
<td>14.8</td>
<td>0.258</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>13.2</td>
<td>14.8</td>
<td>0.547</td>
</tr>
</tbody>
</table>

UARS, upper airway resistance syndrome; chi-squared test ($\chi^2$) $p < 0.05$.

it can be said that the volunteers with UARS has more nasal obstruction, observed during the physical examination, than the volunteers without SRBD.

It is known that not only the alterations detected at the physical examination determine whether or not a patient has nasal obstruction. These findings should always be correlated with clinical symptoms. In the present study, the group with UARS had more complaints of oropharyngeal dryness than the control group, indicative of oral breathing during sleep. Conversely, regarding the clinical complaint of nasal obstruction, the authors did not find a statistically significant difference between the two groups, but rather found a greater tendency for this type of complaint in the group with UARS ($p < 0.11$).

The mouth and oropharyngeal assessment of the study volunteers showed data consistent with the available literature, i.e., low prevalence of micrognathia, ogival hard palate, tonsillar hypertrophy, and large tongue in individuals

Table 4  Logistic regression model of UARS predictors.

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>S.E.</th>
<th>p</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.09</td>
<td>0.03</td>
<td>0.007</td>
<td>1.1</td>
<td>1.0-1.2</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2.41</td>
<td>0.81</td>
<td>0.003</td>
<td>11.2</td>
<td>2.3-54.4</td>
</tr>
<tr>
<td>Altered nose</td>
<td>2.75</td>
<td>0.86</td>
<td>0.001</td>
<td>15.6</td>
<td>2.9-84.0</td>
</tr>
<tr>
<td>Oropharyngeal dryness</td>
<td>2.03</td>
<td>0.82</td>
<td>0.013</td>
<td>7.6</td>
<td>1.5-37.5</td>
</tr>
<tr>
<td>Rhinopathy</td>
<td>-1.85</td>
<td>0.79</td>
<td>0.019</td>
<td>0.2</td>
<td>0.0-0.7</td>
</tr>
<tr>
<td>Constant</td>
<td>-6.56</td>
<td>1.71</td>
<td>0</td>
<td>0.0</td>
<td></td>
</tr>
</tbody>
</table>

UARS, upper airway resistance syndrome; logistic regression test with backward Wald method. Excluded variables: gender, body mass index, web palate, posterior palate, thick palate, ogival hard palate, micrognathia, medialized pillars, tonsil grades 2 and 3, uvula, large tongue, Mallampati grades 3 and 4, AHI.
Orofacial-cervical alterations in individuals

with UARS. These alterations are most frequently observed in patients with OSAS and are not classically associated with patients with UARS. In this regard, it can be said that individuals with UARS are similar to individuals without SRBD.

The investigation of the variable oropharynx alteration in this study showed that both groups had low prevalence of patients with this alteration. This variable, like the altered nose variable, consists in a set of data obtained during the physical examination of the oropharynx, in order to differentiate a normal oropharynx from one disclosing a series of alterations that might be related to SRBD. Many authors believe that oropharyngeal alterations are more related to OSAS that to UARS.

Regarding the other variables measured in this study, results similar to those described in the literature were observed. There were no differences regarding gender and socioeconomic distribution when the two groups were compared. Despite the trend toward a higher percentage of obese individuals in the UARS group (p = 0.06), there was a very small number of volunteers with BMI > 30, and these results are consistent with classic characteristics of patients with UARS who, in general, are not obese. When investigating clinical symptoms related to sleep, the authors observed results consistent with characteristics that are well established in the UARS literature, i.e., increased frequency of insomnia and nocturnal headache complaints in the group with UARS.

The typical respiratory event of UARS is the awakening associated with respiratory effort, or respiratory effort related arousal (RERA). It causes increased UA resistance, generating a progressive increase in inspiratory negative pressure, with concomitant decrease in nasal airflow, without apnea/hypopnea and oxyhemoglobin desaturation, followed by awakening, with immediate decrease in UA resistance. The gold standard for RERA detection is measurement of esophageal pressure by an esophageal balloon that shows a progressive increase in negative intrathoracic pressure that culminates in cortical awakening. This is an invasive and uncomfortable technique, that impairs the onset or maintenance of sleep and, therefore, is not widely used in basal polysomnography literature studies; for these reasons, it was not used in the present study either, which comprises a study limitation.

However, although controversial, some authors maintain that the efficiency of the nasal pressure transducer coupled to the nasal cannula, whether or not associated to a thermistor, may yield a similar result to an esophageal catheter to identify increased respiratory effort and airflow limitation, a technique that is more comfortable and less invasive.

In addition to the study limitation regarding the use of the esophageal balloon, the interpretation and assessment by a physician may introduce a bias. In an attempt to systematize the examination and the classifications to be used, aiming at reducing the bias, only otolaryngologists were recruited to perform patient physical examination, and the number of physicians who assessed patients was also limited (n = 6). Furthermore, prior to patient assessment, the professionals were trained and familiarized with all the classifications used.

The criteria for UARS definition are still controversial in the literature. The lack of a consensus among researchers creates great difficulty in performing studies involving patients with UARS and, consequently, hinders the advance of knowledge about this disease. Nevertheless, this study, using a well-defined UARS criterion, involved an otolaryngological assessment carried out in a population sample representative of one of the most important cities in the world. Therefore, in accordance with these results, the authors believe that, UARS is a multifactorial disease with increased risk of associated comorbidities; however, the nose has a key role in the physiopathology of the disease and should always be thoroughly assessed in a patient diagnosed with UARS.

Conclusions

Systematic assessment of the facial skeleton, mouth, pharynx, and nose in volunteers with UARS and volunteers without SRBD, through orofacial-cervical physical examination in a population sample representative of the city of São Paulo, showed that the presence of UARS is mainly associated with nasal alterations and oropharyngeal dryness, in addition to the risk of high blood pressure, regardless of gender and presence of obesity.

Conflicts of interest

The authors declare no conflicts of interest.

References