Clinical phenotype of South-East Asian temporomandibular disorder patients with upper airway resistance syndrome

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SUMMARY Clinical and radiographic characteristics of a subset of South East Asian temporomandibular disorder (TMD) patients with comorbid upper airway resistance syndrome (UARS) were documented in a multi-center prospective series of 86 patients (26 men and 60 women / mean age 35.7 years). All had excessive daytime sleepiness, high arousal index and Apnoea-Hypopnoea Index (AHI) <5. The mean body mass index was 20.1, mean arousal index 16.2, mean respiratory disturbance index 19.6, mean AHI 3.9 while the mean Epworth Sleepiness Scale was 14.8. Many had functional somatic complaints; 66.3% headaches, 41.9% neck aches, 53.5% masticatory muscle myalgia, 68.6% temporomandibular joint (TMJ) arthralgia while 90.7% reported sleep bruxism (SB). Unlike patients with obstructive sleep apnoea (OSA), hypertension was uncommon (4.7%) while depression was prevalent at 68.6% with short REM latency of <90 min and an increased REM composition >25% documented in 79.6% and 57.6% of these depressed patients, respectively. 65.1% displayed a posteriorly displaced condyle at maximum intercuspation with or without TMJ clicking. Most exhibited a forward head posture (FHP) characterised by loss of normal cervical lordosis (80.2%), C0–C1 narrowing (38.4%) or an elevated hyoid position (50%), and 91.9% had nasal congestion. We postulate the TMD-UARS phenotype may have originally developed as an adaptive response to ‘awake’ disordered breathing during growth. Patients with persistent TMD and/or reporting SB should be screened for UARS and chronic nasal obstruction, especially when they also present with FHP. The lateral cephalogram is a useful tool in the differentiation of UARS from other OSA phenotypes.

KEYWORDS: upper airway resistance syndrome, obstructive sleep apnoea, temporomandibular disorders, persistent oro-facial muscle pain, sleep bruxism, oral appliance therapy

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Introduction

Multiple factors influence the pathophysiology of obstructive sleep apnoea (OSA) and there is not one homogenous Pickwickian phenotype. Craniofacial morphology and non-anatomic factors, like low respiratory arousal threshold, may feature more prominently in certain sleep-related breathing disorders (SDB) (1).

It has been our experience that although the majority of local patients referred for the management of persistent temporomandibular disorders (TMD) had sleep complaints, their polysomnographic (PSG) reports often featured numerous arousals during sleep preceded by increased respiratory effort without significant apnoea or hypopnoea. These patients had characteristic flow limitations and excessive daytime sleepiness that would have qualified them as having an upper airway resistance syndrome (UARS), even though the existence of the latter as a distinct entity continues to be debated. Our observations were
recently corroborated by Dudrovsky et al. (2) who found that myofascial pain in TMD was associated with mild but significant elevation in sleep fragmentation and increased frequency of respiratory effort related arousal (RERA) events. A lower than normal resting arterial blood pressure, cold extremities, orthostatic hypotension, history of fainting, decrease in baro-reflex sensitivity and autonomic dysregulation (with a bias towards enhanced cardio-sympathetic tone) have also been documented in patients with chronic TMD (3) and UARS (4).

Guilleminault and Chowdhuri (5) compared UARS patients with OSA patients and found the former presented with a different phenotype. They posited that craniofacial morphology played a bigger role in UARS than OSA. Most South–East Asian immigrant populations have a common Southern Chinese ancestry. A recent study (6) on a sample of 242 multiethnic Asian adults, aged 21–79 years, who completed home-based sleep testing found a comparatively high estimated prevalence of moderate-severe SDB of 30.5% and mild-moderate SDB of 40.3% in Singapore. The Chinese had the highest rates of SDB amongst the three major ethnic groups even though they had the lowest obesity rates (6). The ‘restricted craniofacial bony enclosure’ (i.e. smaller maxilla, smaller and retro-positioned mandible, and a shorter, steeper anterior cranial base) identified with this ethnic grouping may render South–East Asians more prone to develop SDB (7) in general and UARS in particular.

Patients with UARS are generally younger, less overweight (may be thin or even underweight) or had lower weight gain during the past 5 years compared to OSA patients, and all reported daytime sleepiness or fatigue (8). Unlike the high male-to-female ratio expected in OSA, more pre-menopausal females and children are represented. All other OSA clinical symptoms may also apply to UARS, such as nocturia, nocturnal awakening, sleep inefficiency, insomnia and cognitive impairment; however, headaches, jaw aches and temporomandibular joint (TMJ) clicking with/or without arthralgia, vasomotor/allergic rhinitis, mouth breathing, neck aches, sleep bruxism (SB) and irritable bowel syndrome have also been noted to be more frequent in patients with UARS (8, 9). The symptoms of UARS were similar to those of the functional somatic syndromes (9). Psychological complaints may also be common in these patients, such as difficulty in concentrating and depressive mood, anxiety, impaired daily functioning and poor perception of sleep quality (9).

The relationship between UARS and TMD, however, has not been well researched. The primary purpose of our study was to document the clinical and radiographic presentations of a subset of South–East Asian TMD patients with comorbid UARS. Understanding how anatomic and non-anatomic factors interact would provide us better therapeutic insights when dealing with this unique patient population.

Materials and methods

This was a non-randomised prospective multicentre collection of 86 South–East Asian patients seen in either the ENT (KPP), the Dental (DKLT) Centres and/or a combined ENT-Dental session, who met the selection criteria. All patients had ‘persistent orofacial muscle pain’ and/or met published Research Diagnostic Criteria for Temporomandibular Disorders (RDC-TMD) Axis I physical findings for myofascial pain without/with limited opening (10).

All patients underwent a comprehensive clinical assessment including a thorough physical examination, naso-endoscopy and an overnight home-based wrist-worn WatchPAT 200 sleep test. Arousal index (RERAs) were based on the Respiratory Disturbance Index (RDI) less the Apnoea-Hypopnoea Index (AHI). Arousal Index above 5, with excessive daytime sleepiness, was deemed as abnormal. Patients completed the Epworth Sleepiness Scale (ESS) and a quality of life questionnaire. Medical examination included height, weight, neck circumference, body mass index (BMI), and blood pressure, and an endoscopic assessment of the nasal cavity, posterior nasal space, oropharyngeal area, soft palatal redundancy, uvula size and thickness, tonsillar size and Mallampati grade. Flexible naso-endoscopy was performed for all patients and collapse during a Mueller’s manoeuvre was graded for the soft palate, lateral pharyngeal walls and base of tongue on a 5-point scale. A jaw thrust manoeuvre was performed in all patients during the flexible naso-endoscopy and graded based on estimated movement of the base of tongue forwards, in millimetres. Radiographic examination included a lateral cephalogram (LatCeph) and a cone-beam computed tomography (CBCT), (PaX-Reve3D, VATECH Global, Gyeonggi-do, Korea) scan of the skull with a field of view covering the TMJs, the paranasal sinuses,
as well as the maxilla and mandible. The inclusion criteria were age > 18 years, all BMI, normal AHI (AHI < 5), raised arousal index > 5, raised ESS, tonsil size grade 1–2, all Mallampati grades and patients with no previous nose, mouth and throat surgery. The study protocol and methodology were reviewed and approved by the hospital Ethics Committee/Institutional Review Board (IRB).

The sample characteristics were reported in mean (standard deviation) for continuous variables and number (per cent) for categorical variables.

Results

There were 26 men and 60 women, the mean age was 35.7 ± 14.5 years old, mean BMI was 20.1 ± 3.9. The mean arousal index was 16.2 ± 2.9, the mean RDI and mean AHI were 19.6 ± 4.9 and 3.9 ± 2.0 respectively, while the mean ESS was 14.8 ± 2.3. All of these 86 patients reported excessive daytime sleepiness, poor concentration and some form of irritability.

Many of the patients had significant functional somatic complaints; 57 of 86 (66.27%) had headaches, 36 of 86 patients (41.86%) had neck aches, 53.48% (46 of 86) had masticatory muscle myalgia, 68.6% (59 of 86) had TMJ arthralgia, and 90.69% (78 of 86) reported SB. 65.11% (56 of 86) of these TMD-UARS patients displayed a posteriorly displaced mandibular condyle at maximum intercuspation on the CBCT scan, with or without TM joint clicking. An overwhelming majority of the patients exhibited a forward head posture (FHP) based on the cephalometric analyses described by Rocabado (11); 80.23% had a loss of normal cervical lordosis, 38.37% had a narrowing (<4 mm) of the suboccipital space between occiput (C0) and the first cervical vertebra (C1), and 43 of 86 patients (50%) had an elevated hyoid position that is Hyoidale is on (i.e. flat hyoid triangle) or above (i.e. negative hyoid triangle) a line traced between the inferior-anterior angle of C3 up to retragnathion (RGN). Hyoidale (most anterosuperior point on the hyoid body) is normally 5–7 mm below this line (11).

Typical LatCephs of TMD-UARS patients are shown in Fig. 1. The sensitivity, specificity and positive and negative predictive values of cephalometric parameters in predicting the presence of a posteriorly displaced condyle are tabulated in Table 1.

Of significance, 79 of 86 (91.86%) of these UARS patients had symptoms suggestive of allergic and/or vasomotor rhinitis with evident endoscopic swollen inferior sinus turbinates and/or a deviated nasal septum. Ear symptoms like otalgia, tinnitus and/or ear fullness were less common that is 38 of the 86 patients (44.18%). Unlike patients with OSA, hypertension was uncommon, found in only five of these 86 patients (5.81%). Depression was prevalent at 68.6% (59 of 86 patients). Of interest, 47 of the 59 (79.6%) depressed patients had a short REM latency of <90 min, and 34 of them (57.6%) had increased REM density during their sleep (REM > 25%).

70 of 86 (81.39%) patients had snoring (although not always volunteered as a chief complaint).

Discussion

The majority of our patients with UARS presented with a FHP characterised by a loss of normal cervical lordosis, a C0–C1 narrowing and/or a normal or elevated hyoid position. These novel radiographic findings are in sharp contrast to existing OSA cephalometric literature (12) which espoused that the descent of the hyoid bone predicted severity of the SDB. We propose they represent craniofacial and craniomandibular postural adaptations that have occurred during growth to maintain an awake airway patency because of chronic nasal congestion, whereas the descended hyoid position often described in severe OSA reflected adaptive changes to maintain airway patency during sleep (13). Only eight (9.41%) of our sample had S-H > 120 mm, and only three (3.48%) had MP-H > 24 mm – these are two cephalometric markers used to screen for severe OSA (12).

As passive pharyngeal critical closing pressure (P_{CRIT}) has been recently correlated to the hyoid position (14), it can be inferred that the majority of patients with UARS (i.e. with normal or elevated hyoid positions) had normal or intermediate upper airway collapsibility. This is entirely consistent with previous reports that patients with UARS had upper airway sensitivity close to normal (15) and reduced upper airway collapsibility (16) in comparison with OSA sufferers; making them ideal candidates for oral appliance therapy (OAT) as minimal mandibular advancement is required.

Increased craniovertebral angulation has been positively correlated with nasal airway resistance and the
turbulent component of flow suggesting that head posture was sensitive to fluctuations in airway resistance (17). As individuals with UARS have been documented to have awake upper airway resistances threefold higher than normal subjects and OSA patients (18), the extended natural head posture they exhibit may just be a strategy analogous to an upright version of the sniffing position favoured by the anaesthetist in the sedated patient. To simultaneously maintain awake airway patency and regain a horizontal gaze, the patients with UARS has to habitually adopt a FHP while mouth breathing. Many of our patients also presented with certain characteristic dento-alveolar compensations for example deep

Fig. 1. Lateral cephalogram of patients with UARS showing (a) a loss of normal cervical lordosis, showing a C0–C1 narrowing and an elevated hyoid position (i.e. flat Hyoid triangle), (b) a loss of normal cervical lordosis and an elevated hyoid position (i.e. a negative Hyoid triangle) and (c) a loss of normal cervical lordosis (i.e. kyphosis), a C0–C1 narrowing, and an elevated hyoid position (i.e. a negative Hyoid triangle).
With this added insight, the posteriorly displaced condyle should be looked upon as a physiologic adaptation during growth in response to awake disordered breathing in this subset of patients and not a harbinger for the development of TMJ internal derangements (TMJID). Its occurrence, with or without reciprocal clicking, in most cases, neither justifies nor warrants extensive irreversible occlusal therapy to permanently antero-reposition the mandible. However, in a patient with an already restricted bony enclosure should prosthodontic full mouth rehabilitation or orthodontics be indicated for other legitimate reasons, it may be prudent that these be properly planned such that the iatrogenic intervention would improve any craniofacial skeletal restriction on airway patency or, at the very least, not adversely affect the existing ‘anatomical balance’ as discussed by Isono et al. (21) (Fig. 2).

Lateral cephalometry may prove not only to be clinically useful for the identification of positive responders to OAT (i.e. elevated Hyoid = lower $P_{\text{CRIT}}$), but its documentation of FHP serves notice that this is likely a patient with posteriorly displaced condyle(s). The further forwards the head is postured, the more retruded the mandible becomes as it is attached to the chest via the hyoid musculature (Table 1).

Few topics can stoke more controversy amongst dentists than the management of TMJID. In the early eighties, ‘recapturing’ the anteriorly displaced disc, which was nearly always associated with retruded condyle(s), was thought by certain groups to be the critical issue in the resolution of TMD. Dentists were taught how to perform reductive manipulation procedures for patients who presented with acute TM joint close lock. To biomechanically prevent recurrence of the lock and maintain joint decompression, the anteriorly repositioned mandible had to be kept in this position day and night while the patient healed. Farrar popularised the use of a mandibular repositioning appliance which prevented the mandible from falling backwards during sleep and reinjuring the pain-sensitive neurovascular tissues in the retrodiscal part of the TM joint (22). This nocturnal device incorporated a long palatal extension that made contact with the lingual surfaces of the lower anterior teeth (22). It closely resembled the early customised non-titratable mandibular advancement appliances used for OSA.

Simmons and Gibbs (23), in an MRI study employing anterior mandibular repositioning therapy for
TMD, reported that improvements in patient symptoms were seen even in cases where displaced discs were not ‘recaptured’. Could their clinical success, in part, be due to the fact that they were serendipitously addressing the sleep disruption associated with their patient’s unidentified UARS? For patients in whom moderate upper airway obstruction existed, even modest degrees of mandibular advancement (possibly 25–50% of the patient’s maximum possible protrusion) could be clinically effective, as decreases in $P_{CRIT}$ of only 3–5 cm H$_2$O were required to relieve airflow obstruction during sleep and sedation (24).

Neuroception is a term proposed by Porges (25) describing how in mammals, neural circuits continuously and non-cognitively monitor, the external and internal environments for cues to distinguish whether situations are safe, dangerous or life threatening to facilitate adaptive defence behaviours such as fight, flight or freeze. Stress responses such as reactive tachycardia during sleep, elevated levels of catecholamines and cortisol mediated by the sympathetic nervous system and hypothalamic-pituitary-adrenal axis have been reported in UARS (9) and chronic TMD (3) patients alike. The latter has been known to have single nucleotide polymorphisms (SNPs) in the gene encoding catechol-O-methyl transferase, an enzyme normally involved in catechol metabolism. Those with this genetic variant and comorbid UARS will be left with higher residual levels of circulating catecholamines which, in turn, promote pain sensitivity and proinflammatory cytokine release (26).

Park and Chung (27) found increased ESS and Pittsburgh Sleep Quality Index (PSQI) scores as well as elevated plasma cytokine levels of IL-1β, IL-6, IL-10 and TNF-α in 19% of a group of myofascial patients with TMD, especially those with high disability. Their results suggest that chronic inflammation could be the underlying mechanism for the association between sleep disturbance and persistent TMD (27). Thus in patients with UARS, the nightly airway challenge, in the form of repetitive episodes of progressively increasing inspiratory effort terminated by frequent transient arousals, could over time be responsible for the ‘faulty neuroception’ of their internal environment, gradually shifting their autonomic nervous systems into a continuous state of alert modulated by the sympathetic system, with the progressive withdrawal of the ventral vagal brake (25). Faulty neuroception, according to the Polyvagal Theory (25), can contribute to the maladaptive physiological reactivity (mood changes, depression) and the expression of defensive behaviours commonly observed in individuals with TMD, UARS and functional somatic disorders (9).

A NIDCR-sponsored community-based, multisite project (OPPERA) set up to prospectively investigate risk factors for the onset and persistence of painful TMD found evidence that sleep quality deteriorated before participants developed TMD symptomology.

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Others (2) argue that ‘pain-related decrease in the arousal threshold in myofascial TMD cases may set the stage for more frequent arousals during minor airway narrowing episodes that do not necessarily lead to arousals in (normal) controls’. Sleep disruption may, therefore, hold significant promise as an interventional target in efforts to prevent and epigenetically address chronic pain conditions like ‘persistent’ TMD.

Today, management strategies are based upon evidence-based biopsychosocial medical models that have shifted dramatically from occlusal therapy to the identification of vulnerability alleles, SNPs and the careful study of gene-environment interactions that can influence TMD risk (29). We believe UARS in this TMD subpopulation represents an important ‘pathway of vulnerability’ (26) that must be addressed for successful treatment outcomes.

A new protocol that will combine Dental and ENT approaches is needed to better manage UARS in S.E. Asian populations.

**Study limitations**

There were several limitations related to the fact that ours was not a conventional hospital-based PSG study. We chose the WatchPAT 200, a FDA-approved Level 3 portable diagnostic home sleep study device, over the ‘gold standard’ for the following reasons.

From past experience, perhaps because of their unique personalities and/or inherent low arousal thresholds, a not insignificant number of our patients with UARS, unlike their OSA counterparts, reported great difficulty sleeping during PSG because of the intrusive recording armamentarium and/or environment. Although it might be valuable for CPAP titration purposes to create and study the worst scenario for sleep breathing (i.e. being artefactually coerced to sleep supine during PSG even though it might not be their habitual sleeping posture), minimal disruption was the overriding consideration as our aim was to accurately document important positional strategies (e.g. prone or side sleeping) that might be adopted by these patients. We believed this would be more reliably accomplished with the WatchPAT 200 versus PSG as other than the monitors worn on the non-dominant hand and another small position-detecting electrode above the sternum, there were no uncomfortable belts around the body nor electrodes on the head and face.

Another pragmatic consideration was that few sleep laboratories in Singapore offered oesophageal pressure (Pes) monitoring and not many PSG technicians were familiar with the Stanford University criteria for UARS. The WatchPAT algorithm removed the extrapolation biases of the sleep technician and was less expensive and convenient for the patient as it could be performed unsupervised in the comfort of their own home. The sleep tests were therefore performed without Pes measurement, as we felt that patients would not have slept naturally (hence, confounding our results) with an oesophageal probe inserted during sleep. All our patients, however, complied with the UARS diagnostic criteria that we used as follows: excessive daytime sleepiness, an elevated EEG arousal index and AHI < 5.

Some researchers now believe the 86% of SB episodes occurring during NREM sleep as a consequence of arousals represent an extreme manifestation of the complex physiologic oro-facial motor behaviour possibly related to the homoeostatic maintenance of airway patency (30). Although 90–7% of the patients reported SB, it must reemphasised that masticatory muscle EMG was not measured in our overnight study and most of these SB reports were not verified by subsequent PSG but based upon spouse and self-reports, as well as documented evidence of wear on their current nocturnal occlusal splints. The unreliability of subjective SB reports and secondary occlusal wear is well known, and we do not disagree that PSG remains the gold standard for diagnosing SB (31). Moreover, the contribution of concomitant Awake Bruxism, REM Bruxism and/or Secondary Bruxism in each individual situation was inadequately explored – the significance of which have been well discussed (30).

The sample size of our study (86 patients) also limited our capacity to control for covariance and the conclusions we can draw from our data.

**Conclusion**

It is highly plausible that the TMD-UARS phenotype may have originally developed as an adaptive response to awake disordered breathing during growth. The complex interaction between anatomic and non-anatomic factors in each individual situation offers challenges as well as therapeutic opportunities. All
patients with chronic TMD, persistent oro-facial muscle pain and/or reporting SB should be screened for UARS and chronic nasal obstruction, especially when they also present with FHP. The identification and resolution of co-existing UARS are essential for the successful management of this subset of patients with TMD. The lateral cephalogram is a useful tool in the differentiation of UARS from other OSA phenotypes.

Disclosure
There are no financial disclosures and no conflict of interest for the above authors.

References


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