ORIGINAL ARTICLE

The prevalence of syndrome Z (the interaction of obstructive sleep apnoea with the metabolic syndrome) in a teaching hospital in Singapore

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Background: Syndrome Z describes the interaction of obstructive sleep apnoea (OSA) with the metabolic syndrome.
Purpose of study: A pilot study to determine the prevalence of syndrome Z in a teaching hospital in Singapore.
Methods: Patients (age ≥18 years) recruited for this prospective study had to satisfy three of the following five inclusion criteria: fasting glucose >6.1 mmol/l, blood pressure ≥130/85 mm Hg, HDL cholesterol <1.04 mmol/l in men and <1.2 mmol/l in women, triglycerides ≥1.7 mmol/l, and a waist circumference >102 cm in men and >88 cm in women. All subjects underwent standard overnight polysomnography. Overnight fasting glucose and lipid levels were measured and baseline anthropometric data recorded. All sleep studies were scored and reported by a sleep physician. OSA was deemed to be present if the respiratory disturbance index (RDI) was ≥5, with mild, moderate and severe categories classified according to the Chicago criteria.
Results: There were 24 patients (19 males and five females) of whom 10 were Chinese, eight Malay and five of Indian origin, with one other. Mean age was 48±13.5 years, mean body mass index was 34.9±6.1 kg/m^2 and mean waist circumference was 111.3±15.7 cm. 23 (95.8%) of the patients had OSA with a mean RDI of 39.6±22.4 events/h with 15 patients (62.5%) in the severe category. The five patients who fulfilled all five criteria for diagnosis of the metabolic syndrome had severe OSA.
Conclusion: The prevalence of OSA in our studied population exhibiting the metabolic syndrome is very high. Therefore, a polysomnogram should always be considered for this subset of patients.

Syndrome Z describes the interaction of obstructive sleep apnoea (OSA) with vascular risk factors.[1] These include the quartet of hypertension, central obesity, insulin resistance and hyperlipidaemia, also known as the metabolic syndrome or the insulin resistance syndrome. Each component of the metabolic syndrome has an independent and significant impact on the health status of the individual. However, the morbidity and mortality associated with syndrome Z are probably multiplicative rather than additive. Moreover, OSA is an independent risk factor for cardiovascular disease over and above the components of the metabolic syndrome. Therefore, screening for OSA in addition to the metabolic syndrome would provide extra health benefits. The prevalence of OSA is thought to be about 4%[2] and that of the metabolic syndrome about 20%.[3] The prevalence of syndrome Z in the community has not been looked at to date. The aim of this pilot study, therefore, was to determine the prevalence of syndrome Z in our hospital population and extrapolate this information to the community at large.

METHODS

Study design

This prospective study was conducted between January and March 2005. We recruited adult patients ≥18 years of age either from the diabetic clinic or from the general medical inpatient pool. The inclusion criteria were based on minor modifications of the National Cholesterol Education Program, Adult Treatment Panel III (NCEP ATP III) definition[4 5] of the metabolic syndrome and were as follows:

- a fasting serum glucose >6.1 mmol/l or on oral blood glucose lowering drugs,
- blood pressure ≥130/85 mm Hg or on antihypertensive drugs,
- HDL cholesterol <1.04 mmol/l (in men) and <1.2 mmol/l (in women) or on lipid lowering agents,
- serum triglycerides ≥1.7 mmol/l or on triglyceride lowering agents and
- a waist circumference >102 cm in men and >88 cm in women.

Three of the five criteria had to be satisfied prior to inclusion in the study.

We obtained fasting glucose and lipid profiles in patients who were not previously diagnosed as dyslipidaemic or diabetic, as well as anthropometric data such as height, weight, waist and neck circumference from every subject. The patients then underwent standard overnight polysomnography which included multichannel electroencephalographic (EEG), electromyographic (EMG) and electrooculographic (EOG) recording and respiratory monitoring using a nasal thermistor. All sleep studies were supervised and performed with the Alice 4 recording system (Respironics, Carlsbad, CA, USA). The studies were scored by a single sleep technologist according to the criteria of Rechtschaffen and Kales,[6] after which they were reported by an accredited sleep physician. The patient was deemed to have OSA if the respiratory disturbance index (RDI) was ≥5 and was further classified as having mild, moderate or severe disease based on the Chicago criteria.[7]

Abbreviations: BMI, body mass index; NCEP, National Cholesterol Education Program; OSA, obstructive sleep apnoea; RDI, respiratory disturbance index

Statistical analysis

Data were transferred from data collection sheets to an Excel spreadsheet (Microsoft, Redmond, WA, USA). Simple statistics such as percentages were used to calculate the prevalence.

Ethics

Informed consent was obtained from all patients prior to entry into the study. All patients were given an information sheet detailing the purpose of the study and the study procedure. The study was approved by the Hospital Institutional Review Board and conformed to the principles of the Declaration of Helsinki.

RESULTS

A total of 35 patients were recruited during the study period, but 11 of these failed to attend the polysomnogram. Therefore, 24 patients completed the study and ranged in age from 19 to 71 years old (mean 48 ± 13.5 years). They were predominantly male with a racial distribution different from the population distribution of Singapore (table 1).

The body mass index (BMI) in our cohort of patients put them in the obese category, with a mean waist circumference well above the accepted criteria for the metabolic syndrome (table 1).

Twenty two of our patients had a history of hypertension and were on antihypertensive medication. Similarly, 23 patients had type 2 diabetes mellitus and were receiving treatment. Nineteen patients had dyslipidaemia, of whom 13 were on statins, three were on fibrates, two were both on statins and fibrates and one was on ezetimibe. The mean RDI in the cohort was 39.6 ± 22.4 events/h (range: 5–14.9 (mild disease), 15.0–29.9 (moderate disease) and $\geqslant$30 (severe disease)). Of the 24 patients, 21 (87.5%) had moderate-severe OSA and two (8.3%) had mild disease. Only one patient did not have OSA based on his total RDI (table 1). However, this patient had evidence of mild REM (rapid eye movement)-related OSA.

The five patients who fulfilled all five criteria for the diagnosis of the metabolic syndrome had severe OSA (fig 1). The prevalence of OSA in the entire group was 95.8%.

DISCUSSION

This prospective pilot study showed that the prevalence of syndrome Z was very high in our subjects. Each component of the syndrome has significant effects on the cardiovascular and cerebrovascular systems and thus it is important to treat each individual component in order to reduce morbidity and mortality.

Table 1 Patient characteristics

Age	
Mean (SD)	48.0 (13.5)
Median	49.5
Gender	
Male	19 (79.2%)
Female	5 (20.8%)
Racial distribution	
Chinese	10 (41.2%)
Malay	8 (33.3%)
Indian	5 (20.8%)
Other	1 (4.2%)
BMI (kg/m^2)	
Mean (SD)	34.9 (6.1)
Waist circumference (cm)	
Mean (SD)	111.3 (15.7)
Severity of OSA	
Absent	4.2%
Mild	8.3%
Moderate	25.0%
Severe	62.5%

OSA is a disease characterised by repetitive upper airway obstruction that leads to partial or complete obstruction to airflow, resulting in oxygen desaturation and arousal from sleep. This causes symptoms such as unrefreshing sleep, fatigue, poor concentration and excessive daytime sleepiness. OSA patients are up to sevenfold more likely to have a driving accident than the general population.[8] In addition, there is now ample evidence of independent associations of OSA with systemic hypertension, insulin resistance, ischaemic heart disease and stroke.[9–14] Treatment of OSA, most notably with nasal CPAP (continuous positive airway pressure), has been shown in large studies to decrease cardiovascular morbidity and mortality.[10 15] We suggest, therefore, that every patient with the metabolic syndrome should be screened for OSA, at the very least by taking a sleep history and using the Epworth sleepiness scale. If results are positive, a diagnostic sleep study should be performed. In fact the metabolic syndrome itself could serve as a marker of OSA. A recent study showed that the metabolic syndrome was an independent predictor of OSA.[16] The value, therefore, of diagnosing and treating OSA in patients exhibiting the metabolic syndrome cannot be overstated.

Our diagnosis of the metabolic syndrome was based on the latest available National Cholesterol Education Program (NCEP) criteria.[4] However, since then the International Diabetic Federation (IDF) has proposed a new definition for the metabolic syndrome where the cut-off value for waist circumference is ethnic specific.[17] Moreover, the NCEP ATP III criteria when applied to Asians have been shown to underestimate the population at risk for the metabolic syndrome.[18] Using Asian cut-off values[19] for waist circumference in our study could have possibly increased the number of patients with the metabolic syndrome and consequently syndrome Z.

A limitation of our study is the small number of subjects. However, this is a pilot study and further studies with larger numbers would be needed to derive definitive conclusions. A third of the patients failed to turn up for the sleep study. The reason for this is not clear. It may be partly due to poor local awareness of OSA and its potentially serious implications, educational level, language barriers and local perception. Thus, despite the default rate seeming disproportionately high, we believe that with larger numbers it would be negligible. There is a preponderance of males in this cohort, which reflects the small size of the population. However, due to socio-cultural factors, it is common in Asian societies for females to present less often to their doctors with diabetes or hypertension and hence these diagnoses are often missed.

The racial profile of this cohort does not reflect the normal population breakdown of Singapore.[20] There were fewer Chinese patients than might have been expected because our institution serves a catchments area with a young Malay

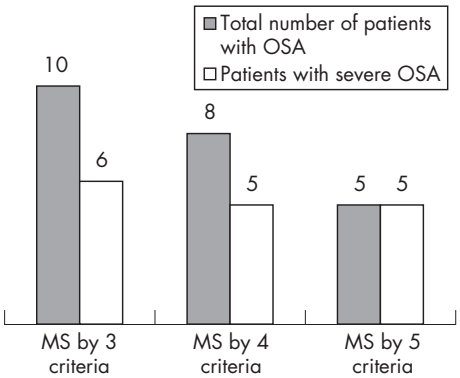

Figure 1 Distribution of metabolic syndrome (MS) by severity.

population and also because the metabolic syndrome may be less prevalent among the Chinese than among the other two racial groups.[21] Certainly, the prevalence of obesity has increased in Singapore in the last 14 years, with 19.1% of the Malay population being obese (BMI $\geqslant$25 kg/m^2). However, this trend has not been noted in other components of the metabolic syndrome, especially blood pressure, which seems to be more prevalent in the Chinese population.[22]

We have already alluded to the fact that patients with the metabolic syndrome should be checked for OSA. Conversely, it is very important and cost-effective for patients diagnosed with OSA to be screened for the metabolic syndrome.

In conclusion, we have shown that the prevalence of syndrome Z in our study population is high. Patients with metabolic syndrome should be screened for OSA by taking a history and, if necessary, by a polysomnogram.

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