Risk factors for developing sleep-disordered breathing in patients with recent ischaemic stroke

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ABSTRACT

Introduction: There are several studies that reported a higher frequency of sleep-disordered breathing (SDB) among ischaemic stroke patients with increasing evidence linking SDB and cardiovascular complications. Many showed prevalence between 43 percent and 72 percent, taking the apnoea-hypopnoea index (AHI) equal to or greater than ten. The main objective of this study was to determine the frequency of SDB in recent ischaemic stroke patients admitted to Hospital Universiti Kebangsaan Malaysia (HUKM) and the relationship between SDB and known risk factors of ischaemic stroke.

Methods: This was a cross-sectional, prospective study involving 28 consecutive acute ischaemic stroke patients admitted to HUKM over three months. Sleep studies were done within one to four weeks after stroke onset. Demographical data and associated risk factors were recorded and data were analysed.

Results: There were 20 men and eight women, with mean age of 60.3 +/- 8.9 years. There were eight Malay, 16 Chinese and four Indian patients. The prevalence of SDB in ischaemic stroke depending on the AHI cut-off was: 92.8 percent for AHI greater than or equal to five, 78.5 percent for AHI greater than or equal to ten, 44.5 percent for AHI greater than or equal to 15, and 37.7 percent for AHI greater than or equal to 20. We discovered that diabetes mellitus and smoking history were important factors predicting significant SDB (AHI greater than or equal to 15) in recent ischaemic stroke cases.

Conclusion: There was a high prevalence of SDB in recent ischaemic stroke patients in HUKM, comparable to other studies. Diabetes mellitus and smoking history were strong predictors of the occurrence of SDB after an ischaemic stroke.

Keywords: cerebrovascular accident, ischaemic stroke, polysomnography, sleep apnoea, sleep-disordered breathing, stroke

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INTRODUCTION

Stroke is the third leading cause of mortality in the world after coronary heart disease and cancer, and the leading cause of morbidity in the western hemisphere [1-2]. Hamidon and Raymond showed that the in-hospital mortality rate of stroke in Hospital Universiti Kebangsaan Malaysia (HUKM) were 11.7% for ischaemic stroke and 27% for haemorrhagic stroke, and that this is relatively similar compared to other studies[3]. The traditional definite, non-modifiable risk factors such as age, gender and race, as well as modifiable risk factors such as underlying hypertension, hyperlipidaemia, smoking, diabetes mellitus (DM) and artherosclerosis, contribute to the incidence of stroke[4-6]. It is well established that the neurological impairment in stroke may disrupt central regulatory centres causing periodic breathing disturbances and the condition has multiple implications on the patients' morbidity and quality of life.

The definitions of sleep-disordered breathing (SDB) are arbitrary but the British Thoracic Society (BTS) National Clinical Guidelines defined an apnoea in adults as a ten-second breathing pause and an hypopnoea as ten-second event where there is continued breathing but ventilation is reduced by at least 50% from the previous baseline during sleep. In some centres, additional criteria such as associated oxygen desaturation or electroencephalography (EEG) arousal are included. SDB is defined by an apnoea-hypopnoea index (AHI) of at least five events/hour of sleep, each lasting for ten seconds or more[7].

The conservative estimate of the prevalence of SDB is reported at up to 4% in the normal population

while the Wisconsin study by Young et al found a prevalence of SDB (with AHI≥15 without symptoms) among the working population (aged between 30 to 60 years) to be 9% in men and 4% in women[8-9]. Among other factors predisposing patients to apnoea and hypopnoea are increasing age, male gender, obesity, sedative drugs, smoking and alcohol consumption[10]. Symptoms are usually non-specific with the dominant symptoms being excessive daytime sleepiness, impaired concentration and snoring. Others include unrefreshing sleep, choking episodes during sleep, witnessed apnoea, restless sleep, personality change, nocturia and decreased libido[7], although not every symptom is present in every case. The sufferer may fail to recognise or underplay some of these symptoms. Therefore, polysomnography (PSG) is usually required to confirm the diagnosis.

The American Sleep Disorders Association review in 1994 categorised sleep study into four types of monitoring: type one being standard full PSG; type two, comprehensive portable PSG, incorporating sleep staging as well as respiratory measures; type three, modified portable apnoea testing using at least three respiratory channels; and type four, continuous single-bioparameter or dual-bioparameter recording, usually either oxygen saturation or airflow. Type one PSG, being the reference standard to which the other monitor types are compared, include oxygen saturation, nasal air flow, ventilatory effort, snoring index, heart rate and features such as electroencephalography, chin electromyography, electrooculography to stage sleep. One or more of these may be omitted in the other limited types of monitoring systems[11].

Several studies have reported a higher frequency of SDB in patients following stroke, with increasing evidence linking SDB and cardiovascular complications. The higher the AHI, the higher the morbidity and mortality related to vascular events. The natural history however, is still unclear, and its relation to post-stroke disability or mortality remains uncertain. In many cases, the SDB patterns in stroke patients seem to be different from classic SDB in the general population. There seems to be a lack of significant sleepiness, poor continuous positive airway pressure (CPAP) acceptance and partial spontaneous improvement with time[12]. There are very limited studies on the natural course of SDB and stroke at present.

Due to the high prevalence of sleep-disordered breathing in stroke patients, the adverse effects SDB has on the quality of life, morbidity and mortality, and its profound implications on patients' care and management, screening for SDB should perhaps be considered as standard work- up in patients with stroke. At present, there is no standard screening technique for SDB as history and symptoms are non-specific. Further work is required to look into this. The main objectives of this study were to determine the frequency of SDB in recent ischaemic stroke patients admitted to HUKM and to determine the known risk factors of stroke that might predict the occurrence of significant SDB in stroke patients.

METHODS

This was a cross-sectional, prospective study involving 28 consecutive acute stroke patients admitted to the medical wards, identified and recruited over a period of three months. The inclusion criteria included patients who were more than 18 years old, who were previously independent with a pre-stroke modified Rankin score of ≤ two, and who had an acute onset of stroke and were admitted to medical wards in HUKM. The diagnoses were based on the Oxfordshire Community Stroke Project (OCSP) classification, which included clinical history, examination and supported by brain computed tomography (CT) / magnetic resonance (MR) imaging findings; namely: total anterior circulation cortical infarct (TAC), partial anterior circulation cortical infarct (PAC) (either middle cerebral artery (MCA) territory or anterior cerebral artery (ACA) territory infarct), lacunar infarct (LAC) or posterior cerebral circulation infarct (POC).

The exclusion criteria included patients who were confused, agitated or those with cognitive impairment in whom sleep study is impractical, patients who already had been diagnosed with sleep apneoa syndromes before from other causes such as significant obesity (BMI >35), clinical hypothyroidism, abnormal facial anatomy such as mandibular deficiency, upper airway tumours, significant neuromuscular and chest wall disorders. Patients who required hypnotics and sedative medications, those who consumed excessive alcohol, those with primary cerebral haemorrhagic stroke and those who were uncooperative and did not sign the informed consent form, were all excluded.

Written informed consent was obtained from patients prior to inclusion into the study. Patient data, which were collected, include: age, race, gender, stroke types (TAC, PCA-MCA, PCA-ACA, LAC or POC infarcts) and risk factors (diabetes mellitus [DM], hypertension, hyperlipidaemia, smoking history, coronary heart disease and previous stroke or transient ischaemic attack [TIA]). Sleep apnoea symptoms prior to stroke, namely: unrefreshing sleep, nocturnal choking, nocturnal coughing,

nocturia, snoring history, witnessed apnoea, early morning headaches, excessive daytime sleepiness and impaired concentration, were recorded. The individual history was taken as positive, if symptoms were observed to be present during sleep on most nights in a week from either a room partner or patient himself. Excessive daytime sleepiness was assessed by asking patients if they felt sleepy or if they fell asleep doing daily activities such as cleaning, cooking, driving a car or at the workplace.

The severity of sleepiness pre-stroke was also objectively assessed using the Epworth sleepiness scale (ESS), whereby patients were asked of his/her chances of falling asleep in eight different situations such as while reading, watching television, talking to someone, sitting inactively, driving a car or as a passenger in a car, or while lying down to rest in the afternoons. The individual situation was scored from zero to three, depending on his/her chances of falling asleep. Each patient was then categorised as either "normal" if the total score was six or less, "sleepy" if the total score was in the range of seven to ten, "very sleepy" with eleven to fifteen, or "dangerously sleepy" if the score was more than sixteen. Height in metres, weight in kilogrammes, body mass index in kg/m^2, neck circumference in centimetres (at the level of the cricothyroid membrane), waist circumference in centimetres (measured midway between the lower rib margin and the superior iliac spine), hip circumference in centimetres (measured at the widest circumference over the greater trochanters) and calculated waist-hip ratios, were recorded.

Severity of stroke was assessed for handicap using the modified Rankin score and functional disability using Barthel index of ADL. Sleep studies were performed using the overnight (10pm - 7am) ResMed Autoset Portable II plus system between week one and week four of stroke onset. Parameters included were airflow by nasal cannulae, arterial oxygen saturation (SaO_2) by a finger pulse oximeter probe, video surveillance or direct observation recorded. Sleep stages were not determined as EEG, EMG and EOG were not measured. Tracings for chest movements and body positions were not recorded. The apnoea score was defined as the number of cessation of nasal air flow for at least ten seconds. Apnoeas shorter than ten seconds were counted if they were followed by an oxygen desaturation of ≥ four percent. The hypopnoea score was defined as a 50% decrease in nasal ventilation for at least ten seconds. Apnoea-hypopnoea index (AHI) - was defined as the frequency of apnoea and hypopnoea per hour of sleep. All data were statistically analysed.

Table I. Demographical data: initial data collection.

Characteristics	Mean ± SD / median (range) at baseline (n = 28)
Weight (kg)	61.0 ± 11.9
Height (m)	1.6 ± 0.1
Body mass index (BMI) (kg/m^2)	23.2 ± 3.9
Neck circumference (cm)	37.8 ± 3.9
Waist (cm)	89.5 ± 9.3
Hip (cm)	95.6 ± 7.9
Waist-hip ratio (WHR)	0.94 ± 0.7
Pre-stroke MRS	0.1 ± 0.5
Modified Rankin score, median (range)	3.5 (1 -5)
Barthel index, median (range)	14 (4 -20)
Epworth sleepiness scale	4 ± 2.7
Apnoea- hypopnoea index (AHI)	17.5 ±11.4

Approval was obtained from the local Research and Ethics Committee prior to the study.

Normally-distributed numerical data were expressed as mean ± standard deviation. Non-normally distributed data were subjected to non-parametric tests and median were used as central measure with ± interquartile range. Univariate analysis was performed on the demographical characteristics and risk factors. This was followed by multivariate analysis and covariates were adjusted for each independent variable. Logistic regression was used to calculate the risk factors for SDB. Any p-value of <0.05 was deemed to be statistically significant.

RESULTS

There were 91 patients admitted to HUKM with acute ischaemic stroke during the three-month recruitment period, the majority of whom were male patients (59 patients or 65%). 40 of the 91 fulfilled the inclusion criteria but only 28 patients gave written consent and returned for the sleep study within one to four weeks of stroke onset. 20 patients (71.4%) were males and eight (28.6%) females. The mean age was 60.3 ± 8.9 years, of whom the youngest patient was 39 years of age. There were eight (28.6%) Malays, 16 (57.1%) Chinese and four (14.3%) Indians. The types of stroke included 39.3% partial anterior circulation infarct involving the MCA territory (PAC-MCA), 57.1% lacunar infarcts (LAC), and 3.6% posterior circulation infarcts (POC).

Vascular risk factors were found in the following proportions of patients: DM 60.7%, hypertension 78.6%, smoking 35.7%, hyperlipidaemia 53.6%, previous stroke or TIA 10.7%, and coronary heart

Table II. Demographial characteristics.

Characteristics		Number (n = 28)	Percentage (%)	Mean ± SD/ median(range)
Modified rankin score (MRS)	0	0	0	3.5 (1 - 5)
	1	7	25	
	2	5	17.9	
	3	2	7.1	
	4	10	35.7	
	5	4	14.3	
Barthel index score of ADL	Very severely disabled (0 - 4)	1	3.6	14 (4 - 20)
	Severely disabled (5 - 9)	5	17.9	
	Moderately disabled (10 -14)	9	32.1	
	Mildly disabled (15 - 19)	3	10.7	
	Physically independent (20)	10	35.7	
Pre-stroke Epworth	Normal	25	89.3	4 ± 2.7
sleepiness score	Sleepy	3	10.7	
	Very sleepy	0	0	
	Dangerously sleepy	0	0	

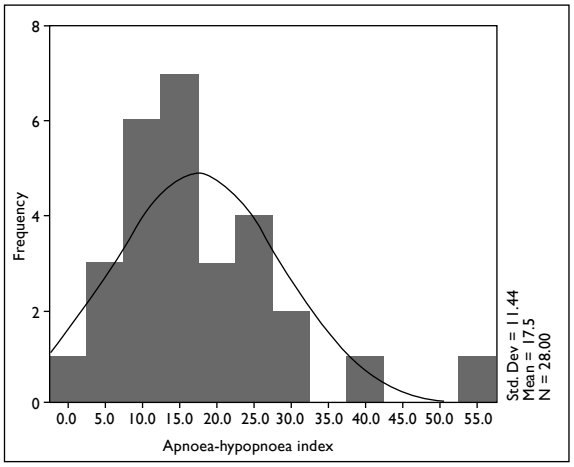

Fig. 1 Frequency of apnoea-hypopnoea index (AHI) in the population.

Table III. Prevalence of SDB according to different AHI cut-offs.

Sleep disordered breathing in acute stroke according to AHI (mean AHI 17.5 ± 11.4)	Frequency n = 28	Percentage (%)
< 5	2	7.1%
≥ 5	26	92.8%
≥ 10	22	78.5%
≥ 15	12	44.8%
≥ 20	10	37.7%

disease 3.6%. The mean weight, height, neck circumference, waist, hip, body mass index (BMI) and waist-hip ratio (WHR) are listed in Table I. Stroke severity, functional status and sleepiness scores were recorded (Table II). The AHI was normally distributed with a mean of 17.5 ±11.4. (Fig. 1) The study showed a significant frequency of SDB among our study patients after ischaemic stroke. This varied depending on the cut-off AHI taken: 92.8% at cut-off ≥ five, 78.5% at ≥ ten, 44.5% at ≥ 15 and 37.7% at ≥ 20 (Table III).

Although there was no significant correlation between gender, race or stroke types and significant SDB, all our patients with LAC infarcts (which formed the majority of infarcts) have SDB at cut-off AHI ≥ five. There was a trend to suggest that the mean AHI was worse in LAC infarcts (18.31 ± 13.4), males (18.3 ± 12.2) and Malay patients (22.1 ± 17.1) compared to other stroke types, gender and race, however none of these associations proved statistically significant ($p > 0.05$) (Fig. 2).

Risk factors were broken down according to AHI levels (Table IV). Multivariate analysis (binary logistic regression) was used to correlate the independent factors associated with significant SDB, based on AHI ≥15. DM (OR 12.0, 95% CI 1.1 – 125.0, p=0.039) and smoking history (OR 9.4; 95% CI 1.1 –

Table IV. Breakdown of independent risk factors according to SDB severity.

Vascular risk factors	Sleep-disordered breathing according to AHI					
	0-4	5-9	10-14	15-19	≥20	Total
Diabetes mellitus	2	1	4	2	8	17
Hypertension	2	3	7	2	8	22
Hyperlipidaemia	0	1	3	1	5	10
History of smoking (ever)	1	2	3	2	6	14
Coronary heart disease	0	0	0	0	1	1
Previous stroke / TIA	1	0	0	0	2	3

Table V. Correlation of independent risk factors with significant SDB using logistic regression.

Vascular risk factors	Significant SDB with AHI ≥ 15			
	Frequency (n = 12)	Odds-ratio (OR)	95% CI	p-value
Diabetes mellitus	10 (83.3%)	12.0	1.1 - 125.7	0.039*
Hypertension	10 (83.3%)	2.1	0.2 - 23.7	0.543
Hyperlipidaemia	6 (50.0%)	1.0	0.1 - 7.7	0.990
History of smoking (ever)	8 (66.7%)	9.4	1.1 - 82.6	0. 043*
Coronary heart disease	1 (8.3%)	3,012.6	0.0 - ∞	0.827
Previous stroke / TIA	2 (16.7%)	4.9	0.3 - 78.8	0.267

* statistically significant

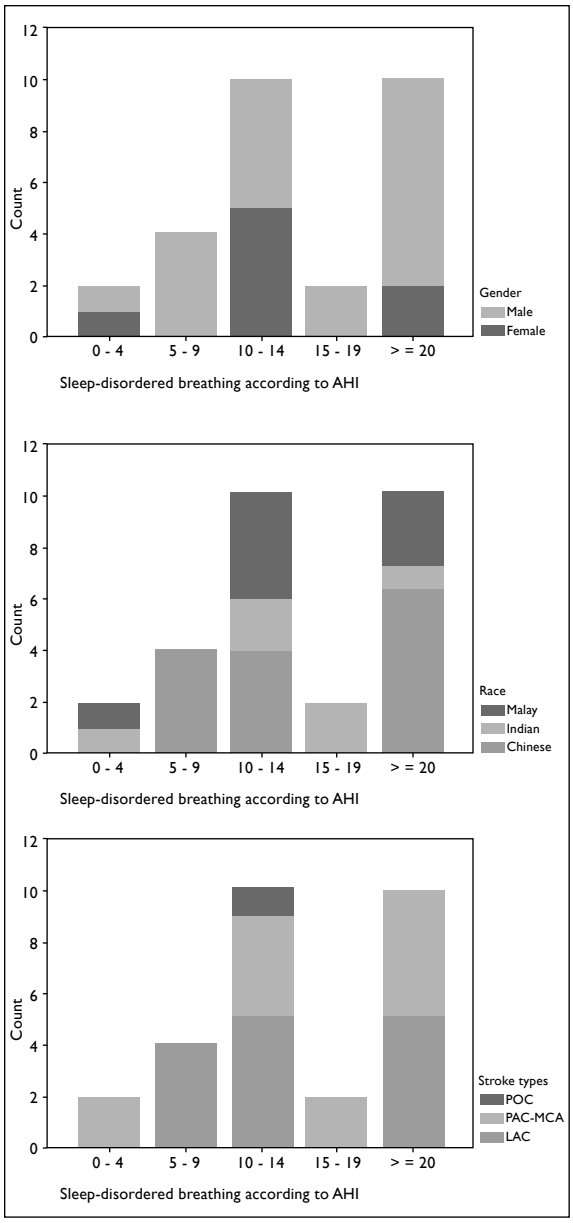

Fig. 2 SDB according to AHI in relation to gender, race and stroke types.

82.6, p = 0.043) were the two vascular risk factors of stroke found to be significant predictors of SDB (with AHI ≥ 15) in stroke patients. Hypertension, coronary heart disease, previous stroke / TIA and hyperlipidaemia were not found to be associated with significant SDB in stroke patients (Fig. 3 and Table V).

We found that a positive snoring history was not statistically significant as a predictor of SDB in our stroke patients (p > 0.05). Despite 26 (92.8%) of the 28 patients having SDB with AHI ≥ five, only 11 of those patients (42.3%) reported a positive history of snoring on most nights in a week prior to stroke. Other factors associated with sleep apnoea, including excessive daytime sleepiness, nocturnal coughing, nocturia and morning headache, were found not to be independently associated with significant SDB (AHI ≥ 15). Eight of the nine patients who did not report any apnoeic symptoms, had SDB with AHI ≥ ten during the sleep study. None of the study patients reported excessive daytime sleepiness, nocturnal choking episodes, impaired concentration or witnessed apnoea pre-stroke.

DISCUSSION

Approximately 0.2% of the population of most Western countries has a stroke each year although reliable information about stroke incidence for non-white populations remains sparse[13-14]. In Malaysia, stroke is the number one killer in those older than 65 years of age[15]. As the quality of life improves, stroke mortality among middle-aged and older people tends to decline and more senior citizens live longer. However, the incidence of stroke will continue to rise. Associated problems such as physical handicap, depression and cognitive dysfunction (including dementia) will pose a higher burden on the government and healthcare system, due to higher costs of treatment and rehabilitation for these patients. Therefore, in order to tackle this, prevention, either primary or secondary, needs to be addressed. High-risk groups and risk factors must be identified and treated.

There were a few well-designed studies that have assessed the frequency of SDB in stroke patients. Several reported a high prevalence varying between 43% and 72% using AHI ≥ ten[16-19]. Dyken et al

(1996) reported SDB prevalence of 77% men and 64% in women with AHI ≥ ten[16]. Mohsenin and Valor determined the prevalence of SDB in ten patients with hemispheric infarcts and found SDB in 80% of patients with a mean AHI of 52[17]. Bassetti et al reported polysomnography data from 13 patients with transient ischaemic attack and 23 patients with stroke investigated at an average of 12 days after the acute cerebrovascular accident. Significant SDB with AHI of 20 or higher was found in 55% of the patients[18]. Wessendorf et al reported SDB prevalence of 61.2% at cutoff AHI ≥ five, 43.5% at AHI ≥ ten, 32% at AHI ≥15 and 21.8% at AHI ≥ 20, involving 147 patients. It was suggested that the lower prevalence was a result of the sleep studies being done much later, at an average of six weeks after stroke onset, instead of the usual third to fourth week[19].

The results of our study further support and extend the observation that the proportion of SDB after ischaemic stroke is much higher than that in the general population, based on historical data. The minor variations between studies can be attributed to the different study designs. Our study obviously had a very small population (n = 28) as a result of strict inclusion and exclusion criteria. Due to a selection bias in selecting less severely-ill patients, our results may represent a "healthier" and atypically younger subgroup of stroke victims. This is reflected by the fact that the mean age of our study population was 60.3 ± 8.9 years old and more than 50% of the patients (18 patients) were below 65 years of age. This, however, seemed to be a notable feature in many studies[16-19]. Harbison et al studied an older and more typical stroke age group with a mean age of 73 ± 9.3 years, quoted a much higher prevalence of SDB involving 68 patients; 96% at AHI cut-off of ten, 84% at 15, 78% at 20 and 42% at 30, with a higher mean AHI of 31 ± 17[20]. There seemed to be an uneven gender distribution in our study population with 59 (65%) male stroke admissions. The female patients also turned out to be more ill and confused with more pre-morbid conditions, and therefore had to be excluded. The fact that the majority of the patients were Chinese only reflected the racial distribution within the hospital's catchment area.

SDB in the normal population without stroke has always been associated with daytime sleepiness, unrefreshed sleep, habitual snoring, early morning headache, and impaired concentration. It would be expected that SDB that may or may not predict a stroke would have similar associations, if not more pronounced. We did not however see a similar pattern in our stroke patients, even with significant SDB by AHI levels. None of the patients reported excessive daytime sleepiness, nocturnal choking episodes, witnessed apnoea or impaired concentration, compared to the pronounced symptoms associated with obstructive sleep apnoea (OSA) seen in the general population without stroke. These probably imply that either sleepiness is not a problem in stroke patients with SDB or that patients were not aware of these problems, possibly due to cognitive deficits after a stroke. Patients' answers were only relative to their own perceptions and were subjected to recall bias. Perhaps this was a weakness in our study as some patients did not have a room partner for questioning. It might also explain the discrepancy between the EES scores and the response from direct questioning about excessive daytime sleepiness. Three out of the 28 patients fell in the sleepy category in the pre-stroke EES score as shown in Table II, despite not reporting any direct excessive daytime sleepiness pre-stroke.

There were high percentages of vascular risk factors of stroke in the population, including hypertension (78.6%), DM (60.7%), hyperlipidaemia (53.6%), smoking history (50.0%), coronary heart disease (3.6%) and previous history of stroke or TIA (10.7%), comparable with other epidemiological data on stroke. We found DM ($p = 0.039$) and history of smoking ($p = 0.043$) to be significantly associated with SDB in stroke. There are increasing clinical-based studies to support the relationship between DM and SDB, be it as a cause or a consequence of SDB or both[21]. SDB promotes insulin resistance, in addition to causing daytime drowsiness and cardiovascular disease[22]. It is thought that sleep deprivation causes an increase in sympathetic nervous system activity and disrupts endocrine functions including insulin secretion and cortisol secretion[23]. At the 98th International Conference of the American Thoracic Society in Atlanta, Resnick hypothesised that breathing abnormalities during sleep, particularly due to central causes, may result in part from autonomic dysfunction, a common complication of DM[24]. The hypothesis is further supported by a report showing that sleep apnoea is more common in diabetic individuals with autonomic neuropathy than in those without[25], and others suggesting a role for autonomic neuropathy in central control of respiration. Two suggestions were offered. Firstly, diabetic autonomic neuropathy may disturb respiratory control by altering central chemoreceptors. Secondly, impaired cardiovascular function (diminished heart rate variability and left ventricular dysfunction) common in diabetic neuropathy may prolong circulatory time and cause a delay in feedback loops involving carbon dioxide

and/or oxygen chemoreceptors in the brain and the heart respectively[26]. All these ventilatory disruptions will be further enhanced in the presence of brain injury following strokes.

We also found that smoking was a significant risk factor for SDB in ischaemic stroke. There is epidemiological evidence linking smoking to SDB. However, unlike DM, there is not much data to support the direct association of smoking as a risk factor for significant SDB in stroke patients. Patients with SDB who smoked have always been advised to stop for general health reasons but there is no evidence that stopping smoking improves apnoeic symptoms. In fact, any weight gain after quitting smoking may worsen SDB. However, there is evidence that cigarette smoking in a healthy population is associated with a decrease in nocturnal oxygen saturation[27-28]. Smoking has been well established as a vascular risk factor for stroke by increasing fibrinogen concentrations, platelet aggregability, haematocrit and reduces fibrinolytic activity. These effects lead to vasoconstriction and therefore reduced blood flow to the brain, giving rise to accelerated thrombus formation and stroke. Smoking too can directly lead to impaired endothelial-dependent vasodilatation. The hypercoagulable state and endothelial dysfunction, which are also seen in SDB patients[29], suggest common associations between smoking and SDB. This theory also explains the possible mechanism for some of the cardiovascular consequences in SDB patients. These effects would be further enhanced in the presence of stroke. Perhaps hypoxia and haemodynamic responses of stroke further contribute to the development of SDB. There certainly is a lot of research still needed in this area.

Would SDB adversely affect the outcome of stroke? Several studies have shown that a higher nocturnal desaturation index was associated with greater mortality and early neurological deterioration, more severe disability and greater mortality after the stroke. Several of the pathophysiological changes that accompany SDB have also been associated with adverse outcome in stroke population. These include large fluctuation in blood pressure in SBD and therefore subsequent correlation with stroke mortality and dependence, cardiac baroreceptor dysfunction associated with higher mortality, recurrent hypoxaemia with frequent apnoea affecting the ischaemic penumbra surrounding the infarcted brain and alternating hypoxaemia and reoxygenation increasing superoxide release, thus adversely affecting stroke patients. Inflammatory and pro-inflammatory markers are also increasingly recognised as possible contributors to vulnerable brain tissue injury[30-31]. Perhaps targeting these patients with pre-stroke OSA for therapy may improve the prognosis associated with SDB as well as stroke outcome, especially since robust evidence shows a significant improvement of symptoms, quality of life and daytime function with treatment of SDB in patients without stroke.

There were limiting factors to this study, including a small study population as a result of poor patient cooperation and short study duration. Timing variations of the sleep study, performed between week one and week four after stroke onset would affect the incidence of the SDB compared to studies with less variability in the timing of the sleep study. Information obtained from the sleep study was limited as our machine only recorded two parameter functions in keeping with the type four level of monitoring according to the American Sleep Disorders Association review[11].

The prevalence of undiscovered SDB following stroke in our patients was high, but comparable to other studies previously done. However, there are no similar published local studies to compare with. Diabetes mellitus and history of smoking predict significant SDB (with AHI ≥15) in ischaemic stroke but not other vascular risk factors of stroke, including hypertension and coronary heart disease. The lack of typical symptoms of sleepiness in SDB with stroke, makes history alone insufficient for diagnosis. Overnight pulse oximetry or limited sleep study may help in screening for SDB, although a normal pulse oximetry cannot be used to rule out SDB. Screening the general population with risk factors for stroke for SDB is not cost-effective either. Perhaps, follow-up of already diagnosed SDB patients and concurrent treatment at the early stages may provide answers to the consequences of SDB over the years. More answers are needed on SDB and its associations, either as a cause or effect, in order to assist management in the future.

REFERENCES

1. Bonita R. Epidemiology of stroke. Lancet 1992; 339:342- 4.
2. Thom JT. Stroke mortality trends: an international perspective. Am Epidemiol 1993; 3:509-18.
3. Hamidon BB, Raymond AA. Predictors of in-hospital mortality after an acute ischaemic stroke. Neurol J Southeast Asia 2003; 8:5-8.
4. Sacco RL. Risk factors and outcomes for ischemic stroke. Neurology 1995; 45 (2 Suppl1):S10-4.
5. Hankey G, Warlow C. Treatment and secondary prevention of stroke: evidence, costs and effects on individuals and populations. Lancet 1999; 354:1457-63.
6. Sacco RL, Wolf PA, Gorelick PB. Risk factors and their management for stroke prevention: outlook for 1999 and beyond. Neurology 1999; 53:15-24.
7. Guideline Development Group. Management of obstructive sleep apnoea/hypopnoea syndrome in adults. A national clinical guideline. Edinburgh: Scottish Intercollegiate Guidelines Network, 2003: 1-38.

8. Young T, Palta M, Dempsey J, et al. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993; 328:1230-5.
9. Strollo PJ, Rogers RM. Obstructive sleep apnoea. N Engl J Med 1996; 334:99-104.
10. Ancoli-Israel S, Kripke DF, Mason W, et al. Sleep apnoea and periodic movements in an aging sample. J Gerontol 1985; 40:419-25.
11. Flemons WW, Littner MR, Rowley JA, et al. Home diagnosis of sleep apnoea: A systemic review of the literature. Chest 2003; 124:1543-79.
12. Hui D, Choy D, Wong L, et al. Prevalence of sleep-disordered breathing and continuous positive airway pressure compliance: results in Chinese patients with first-ever ischaemic stroke. Chest 2002; 122:852-60.
13. Sudlow CLM, Warlow CP. Comparing stroke incidence worldwide: what makes studies comparable? Stroke 1996; 27:550-8.
14. International Society of Hypertension (ISH) Writing Group. ISH: Statement on blood pressure lowering and stroke prevention. J Hypertens 2003; 21:651-63.
15. Members of the expert panel. Consensus Statement on the Management of Ischaemic Stroke. Ministry of Health, Malaysia 2000.
16. Dyken M, SomersV, Yamada T, et al. Investigating the relationship between stroke and obstructive sleep apnoea. Stroke 1996; 27:401- 7.
17. Mohsenin V, Valor R. Sleep apnoea in patients with hemispheric stroke. Arch Phys Med Rehabil 1995; 76:71-6.
18. Bassetti C, Aldrich MS, Chervain RD, et al. Sleep apnoea in patients with transient ischaemic attack and stroke: a prospective study of 59 patients. Neurology 1996; 47:1167-73.
19. Wessendorf TE, Teschler H, Wang YM, et al. Sleep-disordered breathing among patients with first ever stroke. J Neurol 2000; 247:41-7.
20. Harbison JA, Ford GA, James OFW, et al. Sleep-disordered breathing following acute stroke. Q J Med 2002; 95:741-7.
21. Resnick HE, Redline S, Shahar E, et al. Diabetes and sleep disturbances. Diabetes Care 2003; 26: 702-9.
22. Boethal CD. Sleep and the endocrine system: new associations to old diseases. Curr Opinion Pulm Med 2002; 8:502-5.
23. Spiegel K, Leproult R, Van Cauter E. Impact of sleep debt on metabolic and endocrine function. Lancet 1999; 354:1435-9.
24. Resnick HE. NHLBI Sleep Heart Health Study: new dimensions to sleep disordered breathing. Endothelial and SDB. Program and abstracts of the 98th International Conference of the American Thoracic Society, Atlanta; May 2002.
25. Ficker JH, Dertinger SH, Siegfried W, et al. Obstructive sleep apnoea and diabetes mellitus: the role of cardiovascular autonomic neuropathy. Eur Respir J 1998; 11:14-9.
26. Tantucci C, Scionti L, Bottini P, et al. Influence of autonomic neuropathy of different severities on the hypercapnic drive to breathing in diabetic patients. Chest 1997; 112:145-53.
27. Gonzalo CG, Jose AL, Jose MA, et al Cigarette smoking behaviour and respiratory alterations during sleep in a healthy population. Sleep and Breathing 2002; 6:19-24.
28. Guardiola JJ, Fletcher EC, Alhariri H, et al. Hypercoagulability in obstructive sleep apnoea. Clin Pulm Med 2001; 8:238-41.
29. O'Connor GT. NHLBI Sleep Heart Health Study: new dimensions to sleep disordered breathing. Endothelial function and sleep disordered breathing. Program and abstracts of the 98th International Conference of the American Thoracic Society, Atlanta; 2002.
30. Lawrence E, Dundas R, Higgens S, et al. The natural history and associations of sleep disordered breathing in first ever stroke. Int J Clin Pract 2001; 55:584-8.
31. Gibson GJ. Sleep disordered breathing and the outcome of stroke. Thorax 2004; 59:361-3.