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Prevalence and Predictors of Sleep Apnea Risk among Ghanaian Stroke Survivors

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Abstract

Background & Purpose—Sleep apnea has emerged as a potent risk factor for stroke recurrence and mortality. The burden of sleep apnea among stroke survivors in sub-Saharan Africa where stroke incidence and mortality are escalating is unknown. We sought to assess the prevalence of sleep apnea risk and its clinical correlates and predictors among Ghanaian stroke survivors.

Methods—This cross-sectional study involved 200 consecutive stroke survivors attending a Neurology clinic in a tertiary medical center in Kumasi, Ghana. The validated Berlin, STOP-BANG and Epworth Sleepiness Scale questionnaires were administered to all eligible subjects to assess sleep apnea risk and daytime somnolence after collecting demographic, clinical, health-related quality of life, and symptoms of depression using questionnaires.

Results—Median (IQR) age of stroke survivors was 62 (52–72) years and 52.5% were males. 99 (49.5%) subjects were identified as high risk for sleep apnea using the Berlin questionnaire while the STOP-BANG questionnaire classified 26 (13%), 137 (68.5%) and 37 (18.5%) subjects as low, intermediate and high risk for SA respectively. Patients at high risk of sleep apnea were significantly older, used excess alcohol and were less able to perform activities of daily living, although their mean NIHSS scores were significantly lower than those with low risk for sleep apnea. None of the stroke survivors had ever been screened for SA.

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Conceived and designed the experiments: FSS CJ BO

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Conclusions—One out of every two stroke survivors attending a Neurology clinic in Ghana is at high risk for undiagnosed sleep apnea. Greater regional awareness about sleep apnea presence and outcomes among patients and providers is warranted.

Keywords

Sleep apnea; Stroke survivors; Ghana; sub-Saharan Africa; prevalence

INTRODUCTION

There has been a tremendous surge in stroke prevalence over the past four decades in Low-and-Middle Income Countries (LMIC) including sub-Saharan Africa (SSA) [1]. Stroke is a leading cause of death, disability, and dementia globally with 85.5% of stroke burden borne by LMIC [1] with deaths and disability adjusted life years (DALY) lost to stroke at least 7 times higher in LMIC than in high-income countries [2]. This scenario has been engendered by profound escalations in rates of traditional vascular risk factors such as hypertension, dyslipidemia, and diabetes mellitus among adult populations in the SSA [3]. However, the contribution of emerging vascular risk factors such as sleep apnea to stroke burden in LMIC including SSA has not been fully characterized.

Sleep Apnea (SA) has emerged as a potent, independent, and modifiable risk factor for incident stroke and is associated with adverse outcomes among stroke survivors [4–6]. Sleep apnea is characterized by partial or complete collapse of the upper airways during sleep leading to impaired gas exchange and recurrent arousal from sleep. The consequences of SA include excessive daytime sleepiness, cognitive dysfunction, impaired work performance, and impairment in health-related quality of life. An overnight polysomnography (PSG) which measures apnea-hypopnea index (AHI) is the gold standard for diagnosis of SA and is employed to assess severity of SA using AHI cut-offs of 5–15, 15–30, and >30 episodes per hour for mild, moderate, and severe SA respectively. However PSG is time-consuming, expensive, and not readily available, with only 10% of demand for PSG testing in patients with suspected SA being met [7,8]. However the diagnosis of SA can be enhanced by use of validated questionnaires to identify individuals at high risk for further evaluation [9,10].

In resource-replete settings, SA is highly prevalent among stroke survivors with reported frequencies of > 50% among Mexican Americans and non-Hispanic whites [11]. There is however no published study that has assessed the prevalence of SA risk among stroke survivors in sub-Saharan Africa. Our objectives in this study were to assess the prevalence and predictors of SA among Ghanaian stroke survivors attending an outpatient Neurology clinic using the Berlin, STOP-BANG, and the Epworth Sleepiness Scale questionnaires [9,10,12].

METHODS

Study design and setting

This cross-sectional study was approved by the Committee on Human Research Publication and Ethics (CHRPE) of the School of Medical Sciences, Kwame Nkrumah University of

Science and Technology, and the Komfo Anokye Teaching Hospital, (KATH) Kumasi, Ghana. The study was conducted at the Neurology Clinic of the Komfo Anokye Teaching Hospital, a tertiary medical center in Kumasi, Ghana. Kumasi is the second largest city in Ghana, with an estimated population of 4 million inhabitants. The Neurology clinic was established in 2011 and runs once a week receiving referrals for adults >16 years with neurologic disorders from 6 out of the 10 administrative regions of Ghana and serves an estimated population of 10 million as previously described. [13] There are no centers in Ghana for polysomnography services currently.

Study Participants

Consecutive stroke survivors attending the Neurology service at KATH were approached for enrollment into the study after obtaining informed consent. Stroke survivors on sedatives, those with profound aphasia without a proxy, and those who could not stand for measurement of weight due to disability were excluded. Recruitment of study participants was performed from 01/11/2015 to 28/02/2016.

Data Collection

The Berlin questionnaire was administered to all eligible subjects to assess snoring and apneas (Category 1), sleepiness (Category 2), and hypertension and body mass index (Category 3). Subjects were considered high risk for SA if they had a positive score in 2 categories [10]. The STOP-BANG questionnaire is a simple 8-item instrument used to assess symptoms of Snoring, Tiredness, Observed apnea, and a history of high blood pressure as well as Body mass index (BMI), Age >50 years, Neck circumference and Gender. A score of 0–2, 3–4, and 5–8 are classified as low, intermediate, and high risk of SA respectively [14]. The Epworth Sleepiness Scale (ESS) is a validated 8-item questionnaire that measures the ease of falling asleep in the daytime under various circumstances as a measure of daytime hypersomnolence [12]. ESS has been shown to distinguish between patients with primary snoring and SA [12]. A score of 10 is suggestive of SA [15]. These questionnaires were translated into the local dialect (Twi) and administered by two trained Research Assistants and the responses back translated into English and recorded ensuring semantic equivalence.

Demographic information including age, gender, educational status, vascular risk factor profile, stroke type, stroke severity was assessed using National Institute of Health Stroke Scale (NIHSS), functional status assessed using Barthel's index, and Modified Rankin scale were collected by two trained research assistants through review of medical charts and interview of stroke survivors and/or their proxy.

The Center for Epidemiologic Studies Depression Scale [16] and Geriatric Depression Scale [17] were used to screen for depressive symptoms. The Health-Related Quality of Life in Stroke Patients questionnaire [18] was applied to assess the physical, psycho-emotional, cognitive, and socioeconomic domains of quality of life.

Measurements & Definitions

- The weight of study subjects was measured in kilograms using a scale with patient standing at the anatomical position on a scale and the height in

centimeters was measured using a stadiometer with patient standing at the anatomical position in front of the stadiometer. The weight and height measurements were used to calculate the body mass index (BMI). Subjects with BMI $\geq 30\text{kg/m}^2$ were classified as obese [19].

- Neck circumference was measured using a meter tape at the mid-way point of the neck between the mid-cervical spine and the mid-anterior neck to 0.5cm, if palpable, just below the laryngeal prominence. Neck circumference was considered high when it was ≥ 43 cm [20].
- Blood pressure was measured thrice on the upper left arm using a validated automatic sphygmomanometer, after at least 5 minutes of rest and the second and third readings were averaged for analysis. Hypertension was diagnosed if the patient was on antihypertensive medications over the last 15 consecutive days or if the patient had a systolic and/or diastolic blood pressure of 140/90 mmHg.
- Participants were considered to have diabetes mellitus if they were on hypoglycemic medications or if their fasting blood glucose levels were $> 126\text{mg/dl}$ and/or HBA1C $>6.5\%$. [21]
- Dyslipidemia was defined as a high total cholesterol $> 200\text{mg/dl}$ or LDL-cholesterol $> 130\text{mg/dl}$, triglyceride $> 150\text{mg/dl}$ or HDL-cholesterol $<40\text{mg/dl}$ for women and $<50\text{mg/dl}$ for men or previous use of statin for dyslipidemia [22].
- Cardiac disease including myocardial infarction, rheumatic valvular heart disease, and prosthetic heart valve, atrial fibrillation or flutter was based on self-reported history, clinical examination, review of baseline ECG, and/or echocardiography result at enrollment into care at the neurology clinic.
- Current smoking status and alcohol intake status were ascertained from either the patient or a reliable relative. A high alcohol intake was defined as ≥ 14 U per week for women, ≥ 21 U per week for men.
- Physical activity status of participants was assessed using the International Physical Activity Questionnaire. Responders who reported spending more than half the day on their feet or were involved in daily exercises were classified as physically active. Those who spent less than half of the day on their feet or led a sedentary life were classed as physically inactive as has previously been applied.

Statistical Analysis—Stroke subjects were dichotomized into high risk of SA and low risk of SA based on the Berlin questionnaire scores for comparative analysis. Means and medians were compared using the Student's t-test or Mann-Whitney's U-test for paired comparisons. Proportions were compared using the Chi-squared test or Fisher's exact test for proportions with subgroupings <5 . A multivariate logistic regression analysis was performed to identify independent predictors of sleep apnea risk. In all analysis, two-tailed p-values <0.05 were considered statistically significant with no adjustments for multiple comparisons. Statistical analysis was performed using SPSS version 19.

RESULTS

Demographic & clinical characteristics

Two hundred and thirty-four (234) subjects were approached but 34 were excluded due to profound aphasia with no proxy (n=13), declined participation in the study (n=15), or could not stand for anthropometric measurements (n=6), leaving 200 subjects eligible for the present analysis.

Of the 200 stroke survivors, 105 (52.5%) subjects were male and the median (IQR) age of stroke survivors in this survey was 62 (52–72) years. Nearly 50% had no or primary level education and 70% were urban residents. The predominant vascular risk factors identified include hypertension (93%), overweight & obesity (65.5%), dyslipidemia (42.5%), and diabetes mellitus (31.0%). The median (IQR) duration of stroke diagnosis was 2 (1–4) years and stroke was ischemic type in 70%, hemorrhagic in 18%, and the type undetermined in 12% of subjects (Table 1). The median (IQR) NIHSS score and modified Rankin score were 8 (2–12) and 2 (1–4) respectively.

Sleep Apnea Risk

Ninety-nine (49.5%) subjects were identified as high risk for SA by the Berlin questionnaire. Using the STOP-BANG questionnaire 26 (13%), 137 (68.5%), and 37 (18.5%) were classified as low, intermediate, and high risk for SA respectively. Specifically, 63% reported feeling tired or sleepy during the day, 53% reported snoring loudly but only 3% reported breath cessation during sleep using STOP-BANG (Table 2). Using the Epworth Sleepiness Scale, 95 (47.5%) subjects had excessive daytime sleepiness (Table 3).

Correlates of Sleep Apnea Risk

As shown in Table 1, the demographic characteristics, vascular risk factor profile, and clinical features of stroke among those at high risk of SA identified using the Berlin questionnaire were broadly comparable with those at low risk of SA. However, those at high risk for SA were significantly older, were more likely to use alcohol in excess, and were less able to perform activities of daily living on the Barthel's Index scale although their stroke severity on the NIHSS scale was significantly lower than those with low risk of SA. There were no significant differences in rates of depressive symptoms and the domains of health-related quality of life (Table 1).

Predictors of Sleep Apnea Risk

Unadjusted analysis identified age > 60 years, stroke severity measured using the National Institute of Health stroke scale, and alcohol excess as associated with sleep apnea risk. After accounting for covariates, adjusted ORs (95% CI) for age >60 was 2.36 (1.31 – 4.24), $p=0.004$, and for NIHSS score >9/42 was 0.48 (0.26 – 0.87), $p=0.02$, shown in table 4. Sleep apnea risk was not associated with level of hypertension control.

DISCUSSION

Approximately 50% of Ghanaian stroke survivors have a high risk of sleep apnea after an average of 2 years post-stroke. The prevalence of sleep apnea in the present study is comparable to that among Mexican American and non-Hispanic white stroke survivors who were assessed using the Berlin questionnaire [11]. However, amongst Korean (n=293) and Brazilian (n=69) acute stroke survivors, the frequencies of sleep-disordered breathing determined by polysomnography within 1 week post-stroke were 63.1% and 76.8% respectively [23, 24] compared with a rate of 46% among Canadian stroke survivors assessed within 6 months after stroke [25]. It is unknown whether these differences observed in sleep apnea prevalence are due to the divergent methods used for assessing sleep apnea, the populations studied, or the time points after stroke at which sleep apnea was assessed. It is possible that the frequency of sleep apnea is higher at the proximal phases of an acute stroke and attenuates further on. These notwithstanding, the devastating consequences of sleep apnea among stroke survivors has been corroborated in a recent study which reported an almost 10-fold higher mortality risk among stroke survivors with high AHI index compared with those with low AHI index [26]. Thus the present study, which to best of our knowledge is the first among West Africans, has identified a high frequency of sleep apnea risk among stroke survivors who may be at high risk for recurrent cardiovascular events including death. It has been postulated that chronic intermittent hypoxia induced by sleep apnea is associated with inflammation, oxidative stress, insulin resistance, cell apoptosis, vascular endothelial injury, platelet activation, and neuroendocrine disorders which all promote the development of atherosclerosis- the harbinger of cardio-cerebrovascular events. [review by Ma et al. [27]

In our cohort, subjects at high risk for SA were significantly older than those at low risk, with an adjusted OR (95% CI) of 2.36 (1.31–4.24) for SA among the over 60 years than those below 60 years. Previous studies have reported a similar association between increasing age and SA risk [28,29] and it has been postulated to be due to structural alterations in the nasopharynx with ageing [30,31]. There were also some paradoxical observations in this cohort. Firstly, the well-known association between obesity and SA risk [32] was not observed. Further sub-categorization of subjects into low, intermediate, and high risk based on the STOP-BANG questionnaire also failed to reveal significant differences in body mass index. Given the overall low frequency of obesity among the stroke survivors in our cohort, it is possible that other contributing factors such as age and alcohol excess may be stronger determinants of SA risk. Secondly, there were no dissimilarities between SA risk and depressive symptoms and quality of life. It is now recognized that post-stroke depression, obstructive sleep apnea, and cognitive impairment after stroke result in poorer recovery, greater functional impairment, increased stroke recurrence, and mortality even after accounting for traditional risk factors. [33]. Hence although rates of depressive symptoms in our cohort ranged between 50% and 80% based on the two depression screening questionnaires used, depressive symptoms were equally frequent regardless of sleep apnea risk in this predominantly sexagenarian Ghanaian stroke survivors. This could suggest that depressive symptoms may be independent of sleep apnea risk in this population. Thirdly, while subjects with high risk of SA had lower stroke severity than those at lower

risk for SA, those with high SA risk were significantly less able to perform activities of daily living. It is conceivable that among subjects with high risk of SA, daytime somnolence could impair their ability to perform activities of daily living.

Our study is limited by the lack of overnight polysomnographic testing to diagnostically confirm the diagnosis of sleep apnea but this limitation was insurmountable due to the lack of PSG testing facilities in the country, as has been reported in other studies on sleep apnea among non-stroke subjects in sub-Saharan Africa. [34,35] The lack of diagnostic testing together with the absence therapeutic interventions for sleep apnea such as Continuous Positive Airway Pressure devices are crucial gaps in the care of stroke survivors in LMICs where stroke mortality contributes 86% of the global stroke case fatality yearly [1]. Stakeholder engagement with the aim of garnering political will and support to establish sleep diagnostic and treatment centers at regional hospitals in the country would be a starting point to addressing this unmet health need. Secondly, the cross-sectional study design means that the associations observed between sleep apnea risk and clinical and demographic variables cannot be interpreted as causal associations.

Conclusion

In conclusion, sleep apnea risk is high among Ghanaian stroke survivors but this potent risk factor for stroke is not being screened nor treated. Physicians and stroke survivors in the region would benefit from educational interventions to enhance awareness on sleep disordered breathing disorders. Certainly, the conditions are rife for institutional implementation of sleep laboratories for diagnostic and therapeutic interventions to curtail the burden of sleep apnea in developing countries.

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TABLE 1

Comparison of Socio-demographics and Clinical features among Stroke Survivors with High Risk versus Low Risk Sleep Apnea using the Berlin Questionnaire

Variable	High-Risk OSA (n=99)	Low-Risk OSA (n=101)	Total n=200	p-value
Female	48 (48.5)	47 (46.5)	95 (47.5)	0.78
Age, median (IQR)	64 (55–73)	58 (50–72)	62 (52–72)	0.03
Educational level				0.09
None	11 (11.1)	25 (24.8)	36 (18.0)	
Primary	30 (30.3)	26 (25.7)	56 (28.0)	
Secondary	42 (42.4)	35 (34.7)	77 (38.5)	
Tertiary	16 (16.2)	15 (14.9)	31 (15.5)	
Location of residence				0.50
Rural	2 (2.0)	5 (5.0)	7 (3.5)	
Semi-urban	26 (26.3)	28 (27.7)	54 (27.0)	
Urban	71 (71.7)	68 (67.3)	139 (69.5)	
Vascular Risk Factors				
Hypertension	93 (93.9)	93 (92.1)	186 (93.0)	0.62
Diabetes Mellitus	33 (33.3)	29 (28.7)	62 (31.0)	0.48
Dyslipidemia	41 (41.4)	44 (43.6)	85 (42.5)	0.76
Alcohol excess	30 (30.3)	18 (17.8)	48 (24.0)	0.04
Cigarette smoking	4 (4.0)	9 (8.9)	13 (6.5)	0.16
Cardiac diseases	3 (3.0)	0 (0.0)	3 (1.5)	0.08
Physical inactivity	35 (35.4)	37 (36.6)	72 (36.0)	0.85
Normal (BMI <25kg/m ²)	34 (34.3)	35 (34.7)	69 (34.5)	0.72
Overweight (BMI > 25kg/m ²)	40 (40.4)	45 (44.6)	85 (42.5)	
Obesity (BMI >30kg/m ²)	25 (25.3)	21 (20.8)	46 (23.0)	
Body Mass Index (kg/m ²) mean ± SD	27.6 ± 4.9	26.9 ± 4.8	27.2 ± 4.9	0.28
Stroke type				0.58
Ischemic	72 (72.7)	68 (67.3)	140 (70.0)	
Hemorrhagic	15 (15.2)	21 (20.8)	36 (18.0)	
Undetermined	12 (12.1)	12 (11.9)	24 (12.0)	
Duration of stroke in years, Median (IQR)	1.5 (1–4)	2.0 (1–5)	2.0 (1–4)	0.52
NIHSS, Median (IQR)	5 (1–11)	9 (3–14)	8 (2–12)	0.004
Barthel's Index score, Mean ± SD	67.8 ± 33.0	81.8 ± 25.9	74.9 ± 30.4	0.001
Modified Rankin Score, Median (IQR)	2 (1–4)	3 (1–4)	2 (1–4)	0.14
Center of Epidemiological Study	78 (78.8)	79 (78.2)	157 (78.5)	0.92
Depression score 16, n (%)				
Geriatric Depression Scale, n (%)				0.99
0–4 (depression less likely)	42 (42.4)	43 (42.6)	85 (42.5)	
5–9 (suggestive of depression)	49 (49.5)	50 (49.5)	99 (49.5)	
10 (indicative of depression)	8 (8.1)	8 (7.9)	16 (8.0)	

HRQOLISP

Variable	High-Risk OSA (n=99)	Low-Risk OSA (n=101)	Total n =200	p-value
Physical domain (%), median (IQR)	63 (46–83)	60 (46–76)	60 (46–80)	0.36
Psycho-social domain (%), median (IQR)	66 (57–77)	63 (53–73)	63 (54–74)	0.19
Cognitive domain (%), median (IQR)	80 (56–88)	72 (52–88)	76 (52–88)	0.10
Eco-social domain (%), median (IQR)	77 (66–89)	71 (64–81)	74 (66–86)	0.05

CES-D= Center for Epidemiologic Studies Depression Scale, score of >16 is considered depressed. **HRQOLISP**= Health-Related Quality of Life in Stroke Patients questionnaire

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TABLE 2

Frequency of Sleep Apnea Symptoms among Ghanaian Stroke Survivors using the STOP-BANG Questionnaire

Question	Frequency (%) of "Yes" responses
1. Do you Snore loudly (louder than talking or loud enough to be heard through closed doors)?	106 (53.0)
2. Do you often feel Tired , fatigued, or sleepy during daytime?	126 (63.0)
3. Has anyone Observed you stop breathing during your sleep?	6 (3.0)
4. Do you have or are you being treated for high blood Pressure ?	185 (92.5)
5. BMI > 35kg/m ²	12 (6.0)
6. Age over 50 years old?	161 (80.5)
7. Neck circumference > 40cm	19 (9.5)
8. Gender: Male?	107 (53.5)

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Table 3

Comparison of Sleep Apnea risk using the Berlin questionnaire with the STOP-BANG & Epworth Sleepiness Scale

	Berlin questionnaire High-Risk OSA n=99 (49.5%)	Berlin questionnaire Low-Risk OSA n=101 (50.5%)	Total N=200 (100%)	p-value
STOP-BANG				
High risk	28 (28.3)	9 (8.9)	37 (18.5)	<0.0001
Intermediate risk	69 (69.7)	68 (67.3)	137 (68.5)	
Low risk	2 (2.0)	24 (23.8)	26 (13.0)	
Median (IQR) score	4 (4–5)	3 (3–4)		<0.0001
ESS				
High-risk	61 (61.6)	34 (33.7)	95 (47.5)	<0.0001
Low-risk	38 (38.4)	67 (66.3)	105 (52.5)	
Median (IQR) score	12 (5–14)	5 (0–12)	8 (2–13)	<0.0001

Table 4

Multivariate logistic regression analysis for independent predictors of Sleep Apnea risk among Ghanaian Stroke survivors

Variable	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Gender				
Male	0.92 (0.53–1.61)	0.78	–	–
Female	1.00			
Age				
60 years	2.08 (1.18–3.65)	0.01	2.36 (1.31–4.24)	0.004
< 60 years	1.00		1.00	
Body Mass Index				
30 kg/m ²	1.27 (0.67–2.42)	0.46	–	–
< 30 kg/m ²	1.00			
NIHSS score				
9 or more	0.44 (0.25–0.77)	0.004	0.48 (0.26–0.87)	0.02
8 or less	1.00		1.00	
Alcohol excess	2.00 (1.03–3.90)	0.04	1.72 (0.85–3.46)	0.13
Blood Pressure control **				
Uncontrolled BP	0.95 (0.50–1.79)	0.86		
Controlled BP	1.00			

** Blood pressure control defined as Systolic BP and/or diastolic BP of >140/90mmHg