



RISK OF OBSTRUCTIVE SLEEP APNEA SYNDROME IN AN ADULT POPULATION WITH HIV INFECTION IN SOUTHWEST NIGERIA

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ABSTRACT

Background: Emerging data suggest that obstructive sleep apnea syndrome (OSAS) is common among people living with HIV (PLWH). The burden of HIV infection in Nigeria is high. Unrecognized and untreated OSAS have a significant impact on the quality of life and may affect the gains of successful treatment of HIV. The study was carried out to determine the proportion of an adult population of PLWH in South-western Nigeria who have a high risk for OSAS and the associated risk factors.

Study design: A cross-sectional survey of 198 adults attending the clinic dedicated to PLWH at Bowen University Teaching Hospital (BUTH), Ogbomoso was done using the STOP-BANG questionnaire. Data collected include socio-demographic characteristics and anthropometric measurements. The blood pressure and BMI were measured and calculated respectively. Factors associated with high risk for OSAS were identified.

Results: Of the 198 participants, 73.2% were females. Forty (20.2%) had a high risk for OSAS and the factors associated with this risk include male sex, age, BMI, neck circumference, hypertension and use of antiretroviral therapy (ART) regimen containing zidovudine (AZT) and protease inhibitors (PI). Duration on ART and CD4 count did not show a relationship with the risk of OSAS.

Conclusion: The risk of OSAS is high in a significant proportion of an adult population of PLWH in South-western Nigeria and this risk is related to age, male sex, BMI, neck circumference, hypertension and use of ART regimen containing AZT and PI.

Keywords: OSAS, PLWH and STOP-BANG.

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is a sleep-related breathing disorder that is characterized by repeated episodes of upper airway collapse during sleep with associated repeated cycles of desaturation and re-oxygenation, increased sympathetic activity and intra-thoracic pressure changes, leading to sleep fragmentation and consequent daytime fatigue.¹ OSAS has long been recognized as a major contributor to morbidity and mortality in the general population in developed countries. It is an important risk factor for metabolic disease,² cognitive impairment,³ and cardiovascular diseases (CVDs) such as hypertension, myocardial infarction, arrhythmias and stroke.⁴⁻⁹

The prevalence rate of moderate to severe OSAS (apnea-hypopnea index [AHI] ≥ 15 events/hr) varies in the general population but it is estimated to be between 10% and 20%.¹⁰ For instance, in a study done by Adewole et al in Nigeria, a prevalence of 19% was observed.¹¹ This estimated prevalence rate indicates an increase of about 55% over the last 2 decades.¹⁰

Major risk factors for OSAS include male sex, age and obesity. Other risk factors include

adenotonsillar hypertrophy, mandibular retrognathia and micrognathia, genetic syndromes that reduce upper airway patency (e.g., Down syndrome), menopause (in women), and various endocrine syndromes (such as hypothyroidism and acromegaly).^{12,13} Symptoms of OSAS include snoring, insomnia, nocturia, excessive daytime sleepiness, daytime tiredness, morning headaches, cognitive deficits, personality and mood changes, including depression and anxiety. Patients with untreated OSAS have a reduced quality of life and a greater risk of being involved in motor vehicle accidents.^{14,15}

HIV infection which was once regarded as a death sentence is now gradually being seen as a chronic disease.¹⁶ This is as a result of the availability of highly active antiretroviral therapy (ART) for people living with HIV (PLWH) with subsequent dramatically improved survival and life expectancy. This has led to an ageing population of PLWH.¹⁷ As a result of this, non-infectious co-morbidities including metabolic and cardiovascular diseases such as coronary artery disease, diabetes mellitus, and nonalcoholic fatty liver disease are increasingly recognized as important complications of HIV infection and its treatment.^{18,19} A co-morbidity



which has been relatively unexplored in PLWH is OSAS. Emerging data, however, suggests that OSAS is common among PLWH.²⁰⁻²³ Some of the factors that have been attributed to these include; abnormalities of body fat distribution such as central fat accumulation and subcutaneous fat wasting together with adenotonsillar hypertrophy.^{24,23} These abnormalities have been demonstrated to be partly due to the HIV infection and also to ART.²⁵ Unrecognized and untreated OSAS have a significant impact on the quality of life and may affect the gains of successful treatment of HIV.

While many studies on OSAS in Nigeria paid attention to individuals with traditional risk factors like hypertension and diabetes mellitus, data are scarce on the risk of OSAS among PLWH in Nigeria. This is despite the fact that Nigeria has the second-highest burden of HIV infection in the world with an estimated 3.6 million people infected with the virus.²⁶ This study was therefore conceived with the aim of determining the proportion of a sample of an adult population of PLWH in South-western Nigeria who have a high risk for OSAS and the associated risk factors.

MATERIALS AND METHODS

Study area:

The study was carried out at the dedicated clinic to PLWH at BUTH Ogbomoso, Oyo state. The clinic has a population of 220 adults. It holds once every week with an average clinic attendance of 30 patients per clinic.

Ogbomoso is located on latitude 8° 08' 00" East and longitude of 4° 16' 00" North of the Equator.

Ogbomoso is the second-largest city in Oyo State, Nigeria after Ibadan, which is the capital city of Oyo State.

Study design:

The study was a hospital-based cross-sectional descriptive study done over a period of 3 months in the 198 consenting adults attending the clinic and who met the inclusion criteria. Ethical approval was obtained from the Research Ethics Committee of the Bowen University Teaching Hospital, Ogbomoso (NHREC/12/04/2012). The participants were aged 20 to 70 years with a confirmed HIV-positive serology. Excluded were those who did not give consent, those considerably ill to require hospital admission, those who were admitted in the hospital in the last one month, pregnant women, those whose occupations involved taking night-shift and those who were on or had taken sleeping pills in the last one month. The study objectives and procedures were explained to participants and informed consent (written and verbal) obtained.

Other information gathered from the patient's case records included, compliance with clinic

attendance, adherence with medications, history of hospital admission, drug history and antiretroviral therapy regimen (ART) regimen (which may be first line or second line). First line ART regimen includes tenofovir disoproxil fumarate (TDF) plus lamivudine (3TC) plus efavirenz (EFV) or TDF plus 3TC plus dolutegravir (DTG) or abacavir (ABC) plus 3TC plus EFV; while second line ART regimen includes zidovudine (AZT) plus 3TC plus ritonavir-boosted lopinavir (LPV/r) or AZT plus 3TC plus ritonavir-boosted atazanavir (ATV/r). Ritonavir, lopinavir and atazanavir are all protease inhibitors (PI).

Instruments of data collection:

Socio-demographic and clinical data of the study participants were collected using a structured interviewer-administered questionnaire. The questionnaires were administered by Doctors who were trained in questionnaire administration. The weight and height were measured using a GIMA® ASTRA weighing scale with an inbuilt height meter after ensuring that they were minimally dressed (Caps, headgears, wristwatches and foot wears were removed). The BMI (in kg/m²) was calculated using the formula; weight (in kilograms) divided by height² (in meters) and it was classified using the World Health Organization (WHO) classification for overweight and obesity into underweight (<18.5kg/m²), normal weight (18.5 - 24.9kg/m²), overweight (25.0 - 29.9), class I obesity (30.0 - 34.9), class II obesity (35.0 - 39.9) and extreme obesity (≥40).²⁷

The neck circumference was measured by placing a measuring tape directly on the skin at the mid-neck (just below the laryngeal prominence in men) and extending the tape horizontally around the neck with the participant standing upright and facing forwards, with the shoulders relaxed.²⁸

The blood pressure was measured twice at the right arm using an aneroid sphygmomanometer and subsequently finding an average. It was measured with the participant in a seated position with the arm at the level of the heart, using an appropriately sized cuff, after 5 min of relaxation. The blood pressure was classified using JNC VII classification into normal (<120/<80mmhg), prehypertension (120-139/80-89mmhg), stage 1 hypertension (140-159/90-99mmhg), stage 2 hypertension (≥160/≥100mmhg) and isolated systolic hypertension (≥140/<90mmhg).²⁹

The risk of OSAS was assessed using the STOP-BANG questionnaire which is a simple, validated, 8-item instrument, each with a "YES/NO" response related to the clinical features of OSAS, which was developed in response to the need for an easy to use OSAS screening tool.³⁰ The components of the "STOP" aspect of the questionnaire were selected



based on factor analysis of 14 candidate questions intended to reflect snoring, daytime tiredness, observed breathing cessation, and elevated blood pressure. The “BANG” components were chosen based on univariate analysis of the component predictive performance. For each question, answering “yes” scores 1 while a “no” response scores 0. The total score ranges from 0 to 8 and patients are stratified for the risk of OSAS based on their scores. Using a cut off score of ≥ 3 , the questionnaire has the following sensitivity; 84% in detecting any OSAS (apnea-hypopnea index [AHI] > 5), 93% in detecting moderate to severe OSAS (AHI > 15) and 100% in detecting severe OSAS (AHI > 30). A score of 0 to 2 indicates a low risk of OSAS while a score of ≥ 3 indicates a high risk of OSAS.³¹

Data management and analysis

The data obtained were analyzed using the Statistical Package for Social Sciences (SPSS) version 20.0 (SPSS Chicago Inc., IL, U.S.A). Continuous variables were expressed as means \pm standard deviation. Relationship between categorical variables was determined using Pearson chi-square and those between continuous variables were determined using likelihood ratio. A p-value equal to or less than 0.05 was considered significant.

RESULTS

Baseline characteristics of respondents

A total of 198 participants with a mean age of 43.7 ± 10.9 took part in the study. Of these, 145 (73.2%) of them were females. Most of the patients (118/59.6%) were married while 49 (24.7%) were widowed. Fifty-one per cent (101) of the study participants had a CD4 count of over 500 cells/mm³. Ninety point four per cent were on first-line ART regimen and the mean duration of the use of ART was 4.4 ± 3.35 years. (Table I)

Anthropometric characteristics and blood pressure class

The mean BMI of the study participants was 23.54 ± 4.71 with 99 (50%) of them having normal body weight and 53 (26.8%) being overweight. The majority (122 / 61.6%) of the participants had their neck circumference in the range of 30 - 34.9 cm with a mean neck circumference of 33.4 ± 2.97 . Fifty (25.3%) had hypertension. (Table II)

STOP-BANG score

Forty (20.2%) of the participants had a STOP-BANG score of ≥ 3 , implying a high risk of OSAS. Looking at the individual variables of the STOP-BANG score, “age of ≥ 50 years” was the most common variable as it was seen in 67 (33.8%) of the participants. This was however followed by “male gender” and “high blood pressure” which were seen in 26.8% and 21.2% respectively. (Table III)

Relationship between OSAS risk and participants' characteristics

A significant association was observed between the risk of OSAS and the following; age, sex, neck circumference, BMI, hypertension and ART regimen. Duration on ART and CD4 count did not show a significant association with the risk of OSAS (Table IV).

DISCUSSION

Increased recognition and management of OSAS can further help in improving outcomes in the care of PLWH. This study has shown that a significant proportion of PLWH (20.2%) have a high risk of OSAS using the STOP-BANG questionnaire and the factors associated with this risk include age, male sex, hypertension, neck circumference, obesity and use of ART containing AZT and PI. However, CD4 count and duration on ART did not show a significant relationship with the risk of OSAS. The prevalence in this study is less than the 43.6% reported by Njoh et al³² but it is greater than the 7% and 3.9% observed by Epstein LJ et al²³ and Kunisaki et al³³ respectively among PLWH. These various findings can be attributed to the difference in the methodology of the various studies. For instance, while Njoh et al³² used Berlin questionnaire to determine the likelihood of OSAS, Epstein et al²³ confirmed the diagnosis of OSAS using polysomnography (PSG). The different methodologies used in estimating the prevalence of OSAS is largely due to the challenges of carrying out the gold standard diagnostic test PSG on large groups of PLWH. Also, there are limited studies of OSAS in PLWH and this has been corroborated by Owens et al.³⁴ The finding in this present study is however comparable to the 19% observed by Adewole et al in the general Nigerian adult population.¹¹ This may be due to the fact that a majority of the study participants (51%) had a CD4 count of > 500 cells/mm³, suggesting that they are healthy despite living with HIV, hence, comparable with the general population. This similar finding may also not be unconnected with the fact that in this study, the risk of OSAS was not significantly associated with the duration on ART and CD4 count. Use of ART and immune dysfunction, as evidenced by a decline in CD4 count is what makes PLWH unique. Hence, the lack of a significant association between the risk of OSAS and duration on ART together with CD4 count makes the finding in this study comparable to that of the general population. Furthermore, Adewole et al did not find any



association between the risk of OSAS and region of origin in Nigeria, thus making both studies done in different region in Nigeria comparable.

In this study, there was a significant relationship between the risk of OSAS and the age of the participants. This finding corresponds to that of the general population, where it has been established that the prevalence of OSAS increases with increasing age in adults.³⁵ This may be due to age-associated increase in the length of the soft palate, fat deposition around the pharynx and other anatomic changes in structures surrounding the pharynx.³⁶

This study also showed that hypertension was significantly associated with the risk of OSAS. Similarly, this finding is consistent with previous studies in the general population where it has been established that OSAS is an independent risk factor for the development of hypertension.¹ Furthermore, a dose-response relationship has been established between the severity of OSAS and the likelihood of hypertension.³⁷ The blood pressure elevations have been suggested to be due to augmented sympathetic nervous system stimulation secondary to oxidative stress which occurs as a result of the repeated hypoxaemia from the collapse of the upper airway during sleep.³⁸

Obesity and neck circumference also showed a significant relationship with the risk of OSAS. Obesity, particularly, central adiposity has been consistently identified as one of the most important risk factors for OSAS.³⁹ Obesity probably alters the normal upper airway mechanics and aids the pathophysiology of OSAS in different ways including but not limited to parapharyngeal fat deposition and reduction in lung volumes, particularly functional residual capacity.⁴⁰⁻⁴³ Neck circumference has been observed to be a marker of central obesity and a more effective factor in determining the presence of OSAS.^{44,45}

Male sex was also significantly associated with the risk of OSAS. This finding is also in keeping with that of the general population where OSAS has been shown to be more prevalent among males.^{46,47} In fact, male sex is said to be one of the major risk factors for OSAS. Factors responsible for these include the male pattern of body fat distribution (particularly fat deposition in the trunk including the neck), affectation of neurologic control of upper airway-dilating muscles and ventilation by male sex hormones and relatively great pharyngeal length, which exacerbates collapsibility.^{46,47}

In this study, there was also a significant relationship between the risk of OSAS and the regimen of ART. The risk of OSAS was observed to be significantly higher among participants who had AZT and PI being part of their ART regimen. This is likely due to the fact that AZT and PI have been specifically associated with lipodystrophy,^{48,49} which in turn has been associated with the increased prevalence of OSAS among PLWH.²⁴

However, duration on ART did not show a significant relationship with the risk of OSAS. This is despite the fact that ART use has been associated with obesity and lipodystrophy,⁵⁰ which in turn have been associated with the increased prevalence of OSAS among PLWH.²⁴ Furthermore, in this study, there was a significant relationship between obesity and the risk of OSAS. This lack of a significant association between the risk of OSAS and the duration on ART may be because weight gain following commencement of ART is multifactorial with some of the other factors responsible being increasing age and low body weight pre-therapy.⁴⁸ Furthermore, the prevalence and risk factors for overweight and obesity among PLWH has been shown to be similar to that of the general urban population, suggesting that the obesity seen among patients on ART is majorly due to factors seen in the general population rather than due to ART specifically.⁵¹

CD4 count also did not show any significant relationship with the risk of OSAS. This finding has also been corroborated by earlier studies.^{32,33} Our limitations were the unavailability of a sleep laboratory to confirm the diagnosis of OSAS in those with a high risk of OSAS, small sample size and single center study.

CONCLUSION

The risk of OSAS is high among a significant proportion of adults attending the dedicated clinic to PLWH at BUTH Ogbomoso. This risk is significantly associated with age, sex, neck circumference, BMI, hypertension and the use of ART regimen containing AZT and PI. However, duration on ART and CD4 count did not show any significant association with the risk of OSAS.

ACKNOWLEDGEMENTS

We acknowledge the contributions of *Prof OO Adewole, Prof OE Ayodele and Prof PO Akinwusi.*



TABLES

Table I: Basic characteristics of respondents

Sociodemographic profile	Frequency (n)	Percentage (%)
n = 198		
Age in years		
20-30	24	12.1
31-40	61	30.8
41-50	57	28.8
51-60	45	22.7
61-70	11	5.6
Sex		
Male	53	26.8
Female	145	73.2
Marital status		
Married	118	59.6
Single	11	5.6
Divorced	16	8.1
Widowed	49	24.7
Separated	4	2.0
ART regimen		
Firsline	179	90.4
Secondline	18	9.1
Not yet on ART	1	0.5
Duration on ART (in years)		
0-4	114	57.6
5-9	66	33.3
10-14	15	7.6
≥15	3	1.5
CD4 count(cells/mm³)		
>500	101	51.0
350-499	31	15.7
200-349	24	12.1
<200	42	21.2

Table II Anthropometric measurements and pattern of blood p participants

Anthropometric measureme	Frequency (n)	Percentage (%)
n=198		
BMI		
Underweight	29	14.6
Normal weight	99	50.0
Overweight	53	26.8
Class 1 Obesity	11	5.6
Class 2 Obesity	6	3.0
Mean ± SD	23.54±4.71	
Neck circumference		
25.0-29.9	20	10.1
30.0-34.9	122	61.6
35.0-39.9	53	26.8
40.0-44.9	3	1.5
Mean ± SD	33.4±2.97	
Blood pressure class		

Table III: STOP-BANG responses, STOP-BANG score and risk of OSAS

	Frequency (n)	Percentage (%)
STOP-BANG responses*		
Snore	32	16.2
Tiredness	30	15.2
Observed apnoea	3	1.5
Elevated blood pressure	42	21.2
BMI >28 (kg/m ²)	37	18.7
Age ≥50years	67	33.8
Neck circumference >40cm	3	1.5
Male gender	53	26.8
STOP-BANG Score (risk)		
0-2 (low risk of OSAS)	158	79.8
3-8 (high risk of OSAS)	40	20.2

*Multiple responses apply

Table IV: Relationship between participants' characteristics and O

Variables	Risk of OSAS		Test statistic	p-value
	Low n(%)	High n(%)		
n = 158 n = 40				
Age in years				
20-30	22(91.7)	2(8.3)	LRχ ² =	<0.001*
31-40	59(96.7)	2(3.3)		35.523
41-50	46(80.7)	11(19.3)		
51-60	26(57.8)	19(42.2)		
61-70	5(45.5)	6(54.5)		
Sex				
Male	34(64.2)	19(35.8)	χ ² =	0.001*
Female	124(85.5)	21(14.5)		10.991
Neck circumference (cm)				
25-29.9	20(100.0)	0(0.0)	LRχ ² =	<0.001*
30-34.9	105(86.1)	17(13.9)		30.491
35-39.9	33(62.3)	20(37.7)		
40-44.4	0(0.0)	3(100.0)		
CD4 Count				
≥500	77(76.2)	24(23.8)	LRχ ² =	0.074
350-499	23(74.2)	8(25.8)		6.937
200-349	23(95.8)	1(4.2)		
<200	35(83.3)	7(16.7)		
Duration on ART (years)				
0-4	92(80.7)	22(19.3)	LRχ ² =	0.944
5-9	52(78.8)	14(21.2)		0.382
10-14	12(80.0)	3(20.0)		
≥15	2(66.7)	1(33.3)		
ART regimen				
First line	147(82.1)	32(17.9)	χ ² = 7.134	0.008*
Second line	10(55.6)	8(44.4)		
Blood pressure class				
Normal	99(88.4)	13(11.6)	LRχ ² =	0.004*
Prehypertension	26(72.2)	10(27.8)		15.416
Stage 1 hypertension	27(71.1)	11(28.9)		
State 2 hypertension	6(54.5)	5(45.5)		

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