pii: jc-00527-15 http://dx.doi.org/10.5664/jcsm.5926

JCSM
Journal of Clinical Sleep Medicine

SCIENTIFIC INVESTIGATIONS

Restless Legs Syndrome in a Nigerian Elderly Population

Michael B. Fawale, MBBS, FMCP[1]; Isiaka Alani Ismaila, MBBS, FWACP[2]; Adekunle F. Mustapha, MBBS, FMCP[3]; Morenikeji A. Komolafe, MBBS, FWACP[1]; Tewogbade A. Adedeji, MBBS, MPH, FMCPath[4]

[1]Neurology Unit, Department of Medicine, College of Health Sciences, Obafemi Awolowo University, Ile-Ife, Nigeria; [2]Department of Family Medicine, State Hospital, Ilesa, Nigeria; [3]Neurology Unit, Department of Medicine, College of Health Sciences, Ladoke Akintola University of Technology, Osogbo, Nigeria; [4]Department of Chemical Pathology, College of Health Sciences, Obafemi Awolowo University, Ile-Ife, Nigeria.

Study Objectives: The prevalence of restless legs syndrome (RLS) is highest in the elderly in Caucasian populations; the prevalence of RLS in elderly Africans is not known. This study aimed at determining the frequency and associations of RLS in a Nigerian elderly population.
Methods: The study population comprised of 633 consecutive elderly individuals aged 65–105 years attending the general outpatient clinic of the State Hospital, Ilesa, for minor complaints and routine check-up. The diagnosis of RLS was made using the 2003 minimal criteria of the International Restless Legs Syndrome Study Group. Relevant sociodemographic and clinical data, including sleep duration, were also obtained.
Results: Restless legs syndrome was found in 3.5% of the study population with a male-female ratio of 2:1. There was no significant age (p = 0.427) or gender (p = 0.178) influence on the prevalence of RLS except in the 75- to 84-year age group where there was significant male preponderance (p = 0.044). A strong independent association between RLS and sleep duration (OR, 3.229; 95% CI, 1.283–8.486; p = 0.013) and past history of head injury (OR, 4.691; 95% CI, 1.750–12.577; p = 0.002) was found.
Conclusions: Our finding support previous reports of a possible lower prevalence of RLS in Africans. Restless legs syndrome independently increases the odds of habitual sleep curtailment in elderly individuals. Head injury may be a risk factor for future RLS; this requires further investigation as indirect evidence for a possible link between RLS and traumatic brain injury exists.
Keywords: restless legs syndrome, elderly, prevalence, Nigeria
Citation: Fawale MB, Ismaila IA, Mustapha AF, Komolafe MA, Adedeji TA. Restless legs syndrome in a Nigerian elderly population. *J Clin Sleep Med* 2016;12(7):965–972.

INTRODUCTION

Restless legs syndrome (RLS), a sensorimotor disorder of sleep-wake motor regulation, is reported to be common in North America and Europe with a prevalence of 5% to 15% in the general population.[1,2] Its prevalence in Asia, however, varies widely ranging between 0.7% and 12.5%.[3,4,5,6] Emerging data suggest that RLS may not be common in Africa. The only available population-based data from Africa were reported recently in Tanzania, which put the prevalence of RLS in two Tanzanian populations at 0.013% to 0.037% in the general population.[7,8] While a number of studies have demonstrated no increase in RLS prevalence with age, most reports seem to suggest that RLS prevalence is highest in the elderly compared with other age groups.[9] Data from across Europe and North America shows that RLS prevalence increases strongly with age reaching a plateau in the 6th or 7th decade of life when it is 5% to 32.4%.[10] The wide variation in reported prevalence probably indicates differences in population characteristics, sampling frame, and inconsistencies in RLS diagnostic criteria and procedures.[10] In the RLS literature, reports from Africa are scanty with few available prevalence data emerging from East Africa.[7,8] There is a need to generate more information on RLS in Africa. Furthermore, the long term sleep curtailment associated with RLS has profound negative impact on health outcomes.[11] This, coupled with the increased risk of RLS with age, provide ample justification for an investigation into its characteristics in older people. This current study aimed at determining the prevalence of RLS in a primary care population of elderly individuals in Southwestern Nigeria and to characterize its demographic and clinical associations.

BRIEF SUMMARY
Current Knowledge/Study Rationale: Previous reports indicate that the prevalence of restless legs syndrome (RLS) in the African general population is lower compared with Caucasian populations. The prevalence and associations of RLS among elderly Africans are not known.
Study Impact: The findings of this study suggest that the prevalence of RLS among elderly Africans is low and that RLS independently increases the odds of habitual sleep curtailment in elderly individuals. Head injury may be a risk factor for future RLS; this requires further investigation as indirect evidence for a possible link between RLS and traumatic brain injury exists.

METHODS

Participants, Setting and Procedure for Data Collection

The study participants comprised elderly individuals attending the general outpatient clinic, a primary care unit, of the

State Hospital, Ilesa, for routine medical check-up and minor complaints such as symptoms of malaria, lumbar spondylosis, and osteoarthritis. They were 633 consenting individuals (105 male, 494 female) aged 65 to 105 years and were recruited between June 2014 and April 2015. They were to be ambulant, community-living, and of Nigerian origin. They were also to be aged ≥ 65 years and to give their informed consent. Non-ambulant, institutionalized, and non-consenting individuals were excluded. Individuals of non-Nigerian origin and those with mental impairment severe enough to impair simple conversation were excluded as well. The purpose, procedures, and potential benefits of the study, were first explained to the subjects by the interviewer who was either a doctor or a trained research assistant. The subject was required to give an informed consent before he or she was recruited into the study.

Assessment of Sociodemographic and Clinical Characteristics

Sociodemographic data such as age, sex, marital status, highest formal educational level, employment status, average monthly income, and ethnicity were obtained. History of smoking, alcohol, and use of coffee and kolanut were also obtained. Relevant clinical data including history of hypertension, diabetes, stroke, chronic kidney disease, angina pectoris, heart attack, dyslipidemia, and intermittent claudication, were obtained. Also obtained was history of Parkinson disease, migraine and past history of head injury. Medication history and history of oral contraceptive and hormone replacement therapy were obtained from the female participants. Their case records were consulted for corroboration when indicated. The height and weight of each participant were measured by the investigators and trained research assistants in accordance to the World Health Organization (WHO) multinational monitoring of trends and determinants in cardiovascular disease criteria.[12] To measure height, the participant was asked to take off his/her hats or head ties and shoes, stand with his/her back to a vertical rigid measure calibrated to the nearest 0.1 centimeter (cm). They were asked to hold their head and look straight in front of them. A flat rule was placed on the highest point on the participant's head (scalp) at right angles to the vertical rule. The point at which the hand-held rule touched the vertical rule was the participant's height. To measure weight, the weighing scale was placed on a hard, straight surface, and the participants were asked to take off their shoes and empty their pockets and stand on the weighing scale while they looked straight ahead of them. Height and weight were measured to the nearest 0.1 cm and 0.1 kilogram (kg), respectively. Body mass index (BMI), a measure of body adiposity, was calculated using the formula weight (kg) divided by the square of height (meter squared; m^2).[13] Sitting blood pressure was measured after a rest of at least 5 minutes.

Restless Legs Syndrome Case Ascertainment

Restless legs syndrome cases were ascertained by a family physician and trained research assistants using the minimum criteria defined by the International Restless Legs Syndrome Study Group (IRLSSG) which include (1) an urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs; (2) the urge to move or unpleasant sensations begin or worsen during periods of rest or inactivity such as lying or sitting; (3) the urge to move or unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues; and (4) the urge to move or unpleasant sensations are worse in the evening or night than during the day or only occur in the evening or night.[14] Those who fulfilled the 4 IRLSSG minimal criteria were given a diagnosis of RLS. Limited evidence suggests that the IRLSSG minimum criteria have fair sensitivity (86%) but modest specificity (45%).[15]

Assessment of RLS Severity

The severity of RLS symptoms was assessed using the 10-item IRLSSG Rating Scale (IRLS).[16] Answers to the IRLS items were scored from 4 for the first answer (usually "very severe") to 0 for the last answer (usually none). The sum of the item scores served as the scale score (the total severity score), with higher scores representing a more severe disease. The subjects with RLS were then divided into 4 groups based on the severity of their symptoms according to the IRLS score (mild: 0–10, moderate: 11–20, severe: 21–30, very severe: 31–40). The IRLSSG rating scale has shown excellent internal consistency and criterion validity in a large international multicenter study.[16]

Assessment of Sleep Duration

Subjective habitual sleep duration in the previous 1 month was assessed using the first 4 items of the Pittsburgh Sleep Quality Index which include habitual bed time, habitual wake time, how long it takes to fall asleep, and actual sleep duration considering these first 3 items and the times awake in the night for any reason.[17]

Statistical Analysis

The demographic and clinical characteristics of the study participants were summarized using the Student t-test and χ^2 test. Comparison between participants who fulfilled the minimal criteria for RLS (RLS group) and those who did not (no-RLS group) was done using the Student t-test and χ^2 test. Mean habitual sleep duration in the previous one month was compared between the RLS group and the no-RLS group using the Student t-test. A logistic regression model was constructed using RLS status as the dependent variable and variables that were significantly related to RLS on bivariate analysis, as well as age and gender, as covariates. A 5% statistical significance level was chosen. The Statistical Package for the Social Sciences (SPSS), version 16 (SPSS Inc., Chicago, IL, USA) was used for all analyses.

Ethical Clearance

This study was approved by the ethics and research committee of the Hospital Management Board of the State of Osun, Nigeria.

RESULTS

A total of 633 elderly individuals aged 65 years to 105 years participated in the study. The mean age of the participants was 73.1 ± 7.4 years, with the female participants constituting 83.3% (527) of the study population.

Figure 1—Prevalence of RLS by age and gender.

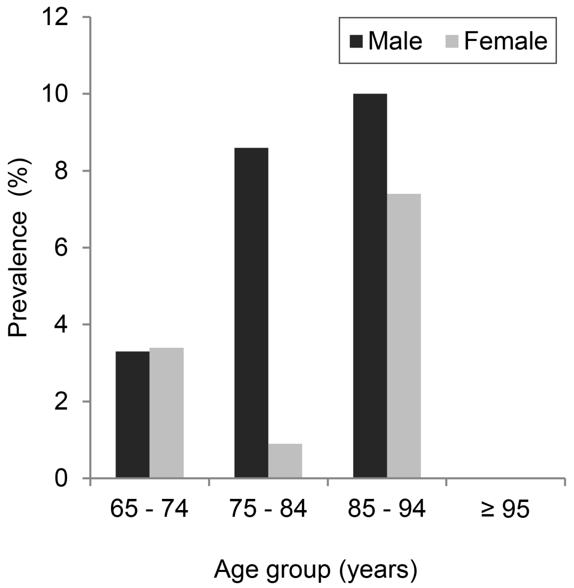
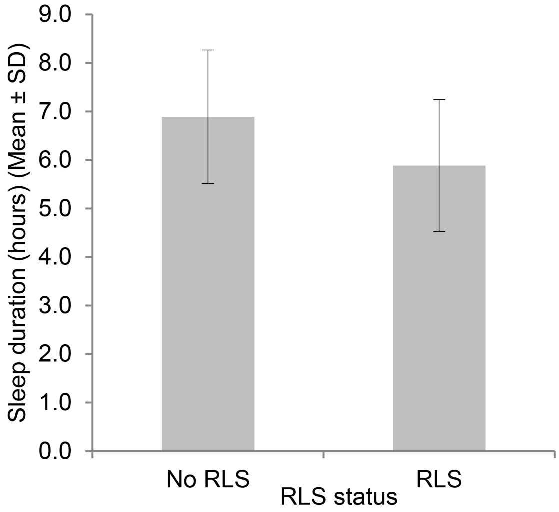


Figure 2—Habitual sleep duration by RLS status.



Prevalence of RLS in the Study Population

Of the 633 participants, 22 (6/106 men, 16/527 women) met the 2003 IRLSSG minimal criteria for RLS translating to a prevalence of 3.5% (5.7% of men, 3.0% of women).

Demographic and Clinical Characteristics of RLS in the Sample

Age and Gender Distribution of RLS in the Sample

There was no significant association between age and RLS prevalence in this population ($p = 0.427$). There was no significant gender difference between participants with RLS and those without RLS ($p = 0.178$). However, there was significant gender difference in the 75- to 84-year age group of participants ($p = 0.044$) (**Figure 1**).

Overall, the frequency of RLS was lowest in the 75- to 84-year age group (2.8%) and highest in the 85- to 94-year age group (8.1%). Similarly, among the female participants, the prevalence was lowest in the 75- to 84-year age group (0.9%) and highest in the 85- to 94-year age group (7.4%). However, the prevalence of RLS among the male participants was steadier, as it ranged from 3.3% in the 65- to 74-year age group to 10.0% in the 85- to 94-year age groups. There was no RLS found in the ≥ 95-year age group. There was no significant age difference between the RLS and no-RLS participants.

Other Demographic Characteristics

All the participants in this study except one were of Yoruba ethnic extraction. About three-fifths of the study population had no formal education. This was the case for the RLS and the no-RLS groups ($p = 0.826$). There was no significant difference between the RLS and the no-RLS groups in terms of smoking history, alcohol history, or kolanut and coffee consumption (**Table 1**).

Clinical Characteristics

Hypertension was the predominant comorbid condition occurring in 72.7% and 79.4% of the RLS and the no-RLS participants, respectively ($p = 0.216$). The RLS and the no-RLS groups did not differ in the frequency of diabetes ($p = 0.710$), stroke ($p = 0.302$), and intermittent claudication ($p = 0.457$). One participant had a past history of heart failure; none had a history of ischemic heart disease, myocardial infarction, dyslipidemia, or chronic kidney disease. Sixteen (72.2%) of the participants with RLS and 80.4% of the no-RLS participants had, at least, one cardiovascular disease ($p = 0.397$). While migraine was reported by 4 (0.6%) of the study participants, none had a history of Parkinson disease. There was no significant difference between RLS and no-RLS participants in terms of body mass index, systolic and diastolic blood pressure, pulse pressure, and mean arterial blood pressure. There was significant difference ($p < 0.001$) in the report of past head injury between the RLS (35.0%) and the no-RLS (10.0%) groups. Report of past head injury was independently associated with increased odds of RLS on regression analysis using age, sex and sleep duration as covariates. The odds of RLS in participants with a past history of head injury was about 5 times compared with those without head injury (OR, 4.691; 95% CI, 1.750–12.577; $p = 0.002$) (**Table 1**). Of those with past history of head injury, 50% and 36.8% of the RLS and non-RLS participants reported loss of consciousness following the head injury, however, report of loss of consciousness following head injury did not significantly relate to RLS ($p = 0.662$).

RLS and Sleep Duration

The participants with RLS had significantly shorter habitual sleep duration in the previous month compared with the non-RLS participants (5.9 ± 1.4 h vs 6.9 ± 1.4 h, $p = 0.001$) (**Figure 2**). A larger proportion of the participants with RLS (42.9%) compared with the non-RLS participants (16.4%) slept habitually for < 6 h ($p = 0.002$). Sleep duration was inversely and independently associated with increased odds of RLS on logistic regression using age, gender and past history of head

Table 1—Demographic and clinical variables by RLS status.

Variable	All	RLS	Non-RLS	p[a]
Age (years) (mean ± SD)	73.1 ± 7.4	73.4 ± 6.9	73.1 ± 7.4	0.849
Sex n (%)				
Male	106 (16.7)	6 (27.3)	100 (16.4)	0.178
Female	527 (83.3)	16 (72.7)	511 (83.6)	
Education (none) n (%)	372 (60.4)	14 (63.6)	358 (58.9)	0.826
Ethnicity (Yoruba) n (%)	631 (99.8)	22 (100)	607 (99.8)	1.000
Smoking n (%)	46 (7.4)	1 (4.5)	45 (7.5)	1.000
Alcohol n (%)	91 (14.4)	5 (22.7)	86 (14.1)	0.261
Coffee n (%)	23 (3.7)	1 (5.0)	22 (3.6)	0.534
Kolanut n (%)	122 (19.4)	7 (31.8)	115 (18.9)	0.134
Hypertension n (%)	501 (79.1)	16 (72.7)	485 (79.4)	0.216
Diabetes n (%)	45 (7.2)	1 (4.8)	44 (7.3)	0.710
Stroke n (%)	10 (1.6)	1 (4.5)	9 (1.5)	0.302
Intermittent claudication n (%)	70 (11.7)	3 (16.7)	67 (11.6)	0.457
Other CVDs[b] n (%)	0 (0)	0 (0)	0 (0)	–
At least one CVD n (%)	507 (80.1)	16 (72.2)	491 (80.4)	0.397
Parkinson disease n (%)	0 (0)	0 (0)	0 (0)	–
Migraine n (%)	4 (0.6)	1 (4.5)	3 (0.5)	0.133
Head injury n (%)	63 (10.5)	7 (35.0)	56 (10.0)	0.000
Associated LOC n (%)	17 (38.6)	3 (50.0)	14 (36.8)	0.662
Oral contraceptive pills n (%)	33 (7.2)	1 (6.2)	32 (7.2)	1.000
BMI (kg/m^2) (mean ± SD)	25.2 ± 5.2	23.8 ± 5.8	25.2 ± 5.2	0.201
SBP (mm Hg) (mean ± SD)	141.0 ± 25.6	136.8 ± 27.3	141.2 ± 25.5	0.433
DBP (mm Hg) (mean ± SD)	83.9 ± 14.7	82.1 ± 11.4	83.6 ± 13.7	0.605
PP (mm Hg) (mean ± SD)	57.5 ± 17.0	54.8 ± 18.7	57.6 ± 17.1	0.448
MAP (mm Hg) (mean ± SD)	103.2 ± 16.9	100.3 ± 16.1	102.8 ± 16.7	0.494

[a]p value of the difference between participants with RLS and those without. [b]Includes coronary artery disease, myocardial infarction, dyslipidemia and chronic kidney disease. RLS, restless legs syndrome; CVD, cardiovascular disease; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial blood pressure; LOC, loss of consciousness.

injury as covariates. The odds of RLS in those who slept habitually for < 6 h was 3 times compared with those who slept ≥ 6 h (OR, 3.229; 95% CI, 1.283–8.486; p = 0.013) (**Table 2**). There was no difference between them in terms of habitual sleep latency (36.7 ± 31.8 vs 31.3 ± 37.7, p = 0.549).

Profile of RLS Severity

Most (76.2%) of the participants with RLS symptoms had a moderately severe disease, 4.8% and 19.1% had mild and severe RLS respectively. Symptom frequency was at least 2 times per week in 90.5% of the RLS participants. There was no significant association between RLS severity and the demographic and clinical characteristics of the participants. There was neither significant association between RLS severity and habitual sleep duration (p = 0.422) nor between RLS severity and report of head injury (p = 0.482) (**Table 3**).

DISCUSSION

Prevalence of RLS in the Study Sample

The prevalence of RLS in this Nigerian primary care sample of community-living elderly individuals was 3.5%. There appears to be significant geographic and racial differences in RLS prevalence with the highest prevalence rates reported from North America and Europe and much lower rates from Asia.[9] Data from Africa is scanty in the RLS literature; we found four published full reports from sub-Saharan Africa (SSA), two of which were population-based[7,8] and conducted in Tanzania, while the rest were hospital-based and targeted people with specific medical conditions.[18,19] Overall, the data from these studies suggest that the prevalence of RLS in sub-Saharan Africa is low compared with other regions of the world.

At first look, compared with the population-based data from Tanzania, the prevalence of RLS in our study would appear much higher. However, the study population and design in these studies differed significantly from ours. Our study focused on people aged 65 years and older, with a mean age 73.1 ± 7.4 years, the Tanzanian studies recruited much younger subjects (14 years and above with mean ages of 32.6 ± 14.7 and 34.6 ± 17.8, respectively). Subgroup analysis revealed that no case of RLS in the ≥ 65-year age range was found in both studies. This finding could suggest that the prevalence of RLS in the elderly population was lower than the general population or that the elderly were underrepresented in the study. In

Table 2—Logistic regression between RLS and demographic and clinical variables.

Variable	OR	95% CI	p
Age (years)	0.990	0.937–1.048	0.723
Sex	0.767	0.258–2.2 48	0.633
Sleep duration < 6 hours	3.229	1.283–8.486	0.013
History of head injury	4.691	1.750–12.577	0.002

Table 3—Demographic and clinical characteristics of the participants by RLS severity.

Characteristic	Mild-Moderate (n = 17)	Severe (n = 4)	p value
Age (years) (mean ± SD)	73.9 ± 6.6	70.8 ± 8.5	0.415
Sex (Female) n (%)	12 (66.7)	4 (100.0)	0.541
Sleep duration (hours) (mean ± SD)	6.0 ± 1.4	5.4 ± 1.1	0.422
BMI (kg/m^2) (mean ± SD)	23.1 ± 5.9	26.6 ± 4.1	0.274
SBP (mm Hg) (mean ± SD)	138.9 ± 28.3	127.5 ± 23.6	0.464
DBP (mm Hg) (mean ± SD)	82.5 ± 11.7	80.0 ± 11.6	0.714
PP (mm Hg) (mean ± SD)	56.4 ± 19.4	47.5 ± 15.0	0.402
MAP (mm Hg) (mean ± SD)	101.3 ± 16.5	95.8 ± 15.0	0.511

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; MAP, mean arterial blood pressure.

comparison with our finding, the prevalence of RLS among the elderly in those populations appears much lower.

Furthermore, there were other important methodological differences between our study and the Tanzanian studies. The latter used a more rigorous method of case ascertainment, going beyond screening with the IRLSSG minimum criteria.[11]

However, in spite of the high prevalence found in our sample of elderly Nigerians compared with the Tanzanian studies, it is lower than the prevalence of RLS in elderly individuals reported from Caucasian populations in which the 2003 IRLSSG minimum criteria were used.[9,20] Comparison with Asian populations is difficult as there is wide variation in the reported prevalence from Asia.[3–6] The prevalence found in this study is much lower than that found in a Korean population of elderly individuals (8.3% and 9.7%),[6,21] but higher than the findings reported from Japan (1.06%),[4] China (0.69%),[5] and Singapore (0.6%),[3] respectively. Further epidemiological studies may be required in Asia, and much more so in Africa, to make reliable inferences on the prevalence of RLS in these regions.

We also found full reports of two hospital-based studies conducted in Sub-Saharan Africa which focused on the prevalence of RLS in individuals with specific disease conditions. One of the studies,[16] carried out on a sample of Nigerians with end-stage renal disease (ESRD), found an RLS prevalence of 5.9%. This is, expectedly, higher than the finding in our study as data from previous studies suggest that ESRD might be a more important risk factor for RLS than age.[9,22] However, the prevalence of RLS in Nigerian ESRD patients was lower than most similar studies[23–25] conducted in other parts of the world which have commonly reported prevalence rates above 20% and high as 83%. This is consistent with the general observation that the prevalence of RLS in Africa may be lower compared with other regions of the world.[7–9] The other hospital-based study,[15] which focused on individuals with chronic pain in a tertiary care center in Mozambique, found a prevalence of RLS of 6.77% in this population. Although the sample was younger than ours, it found a higher prevalence probably due to its high burden of medical morbidities including cancer as well as neuropathy, depression, and hypertension, which have been associated with RLS.[17,24,25]

Age and Gender Distribution of RLS in the Study Sample

While, overall, there was no significant gender difference between subjects with RLS and those without RLS in this present study, male gender was significantly associated with increased odds of RLS in the 75- to 84-year age group. Of particular significance is the gender distribution of RLS in this present study, as the male-to-female ratio is about 2:1. This is inconsistent with what has been reported in most studies. While a few studies have reported a higher prevalence among men or no difference, the prevalence in most studies is approximately twice as high among women as in men.[9] This pattern appears to cut across Europe, North America, and Asia.[9] In the two population-based studies conducted in Tanzania, all the participants with RLS were women.[7,8] In the elderly population, the pattern appears to be similar with most reports showing a two-fold prevalence among elderly women compared with men.[4,6,9] The proportion of men in our sample was limited (16.7% of the study sample) and is not representative of the male-female ratio of the elderly population in Nigeria (1.033:1) nor that the state of Osun (1.030:1) where this study was carried out.[26] It is rather reflective of the elderly population in the primary care clinic where the study was carried out. Our finding in this present study, therefore, requires corroboration with larger studies with larger representation of male participants in other to determine the gender distribution of RLS among elderly Africans.

RLS and Habitual Sleep Duration

In the present study, RLS was independently associated with shorter sleep duration when age, gender, and past history of head injury were adjusted for. Our finding is consistent with reports from observational studies suggesting significant and inverse association between sleep duration and RLS. Innes et al., in a study of an Appalachian primary care population of adults with a mean age of 47.33 years, found a strong inverse association between RLS and sleep duration.[27] While the participants with RLS in that study were older than non-RLS participants, sleep duration remained significantly associated with RLS when age and other potential confounders were adjusted for. In the RLS epidemiology, symptoms, and treatment (REST) study, which recruited participants from the United States and across Europe, more than 75% of the participants with RLS reported at least one sleep-related symptom including insufficient hours of sleep, inability to fall asleep, and inability to stay asleep.[28] A recent basic science research study found significant sleep fragmentation in a *Drosophila* model of RLS, corroborating the findings of previous epidemiological studies.[29]

Sleep disruption is an expected association of RLS, as the urge to move the limbs and the associated unpleasant sensation have the potential to prolong sleep latency and cause frequent arousals.[3] Chronic sleep curtailment and its attendant associations, such as chronic altered daytime functioning are the major immediate potential consequences of RLS.[27,30] These may contribute to the increased risk of poor psychosocial functioning and poor cardiovascular health outcomes that have been demonstrated in individuals with RLS.[17,18]

Report of Past Head Injury and RLS

In this study, we also found a strong association between past head injury and RLS ($p < 0.001$). In the RLS literature, head injury has rarely been reported or investigated as a possible risk factor for RLS. However, studies of sleep in individuals with traumatic brain injury (TBI) suggest that approximately 46% of individuals with chronic TBI have sleep disorder.[31] However, RLS is not listed as one of the common TBI-associated sleep disorders.[27]

Substantial evidence exists, albeit indirect, that may suggest a possible link between TBI and RLS. Impaired dopamine neurotransmission and iron metabolism are thought to be the primary mechanisms underlying at least some cases of RLS. Traumatic brain injury has also been shown to be characterized by impairment of dopamine neurotransmission. Structural imaging suggests that TBI may be associated with disruption of neuronal networks, including the nigrostriatal dopaminergic pathway. A single-photon emission computer tomography (SPECT) study revealed significant striatal dopamine transporter (DAT) deficit in patients with traumatic brain injury.[32] Considerable evidence also exists that disturbances in dopamine neurotransmission contribute to the frontal lobe dysfunction that often complicates traumatic brain injury.[33] Furthermore, interventions that modify dopamine availability in the brain have been shown to improve outcome after TBI. Amantadine has been shown in several clinical trials and in animal research to improve functional recovery after TBI, possibly through its dopamine activity-promoting effect by facilitating pre-synaptic release and blocking post-synaptic reuptake of dopamine.[34,35] Based on evidence from epidemiological and basic science studies, head injury is considered a susceptibility factor for Parkinson disease, which is thought to share pathophysiological pathways with RLS.[36] This body of evidence and the finding of our study provide ample justification for further investigation into a possible association between traumatic brain injury and RLS.

We found no association between RLS and history of cardiovascular disease or other medical comorbidities. Also, there was no association between participants' current blood pressure or body mass index (BMI) and RLS. Restless legs syndrome was also not associated with tobacco smoking, alcohol, or use of coffee or kolanut.

Limitations

The evidence from this study is limited by the following: this study did not differentiate the identified cases of restless legs syndrome into idiopathic and secondary cases. Furthermore, the subjects were not evaluated for certain well-documented risk factors for RLS such as polyneuropathy and low plasma ferritin. Elderly men in this study were underrepresented and this may have contributed to the inverse male-to-female ratio found in the prevalence of RLS. The case ascertainment in this study was limited to the IRLSSG 2003 minimal criteria, which have been shown to have a modest specificity.[15] The temporal relation of head injury reported by some of the participants to the onset of the symptoms of RLS was not determined in this study, limiting conclusions on a possible cause-effect relationship.

CONCLUSIONS

Our study confirmed that the prevalence of RLS may be lower in Africans than Caucasian populations. We found an unusual female-to-male ratio of 1:2, as against 2:1 that has been reported in several studies. This present study also confirmed that RLS is independently and inversely associated with habitual sleep curtailment. Head injury, in this study, was directly, strongly, and independently associated with RLS. Large population-based studies with samples representative of the age and gender distribution in the population, are required to determine the prevalence of RLS in Africa. Further investigation into the relationship between the risk of RLS in individuals with past traumatic brain injury is also required.

ABBREVIATIONS

BMI, body mass index
CI, confidence intervals
cm, centimeter
DAT, dopamine transporter
ESRD, end-stage renal disease
IRLS, International Restless Legs Syndrome Study Group Rating Scale
IRLSSG, International Restless Legs Syndrome Study Group
kg, kilogram

m^2, meter squared
OR, odds ratio
REST, RLS epidemiology, symptoms, and treatment
RLS, restless legs syndrome
SPECT, single-photon emission computer tomography
SPSS, Statistical Package for the Social Sciences
SSA, sub-Saharan Africa
TBI, traumatic brain injury
WHO, World Health Organization

REFERENCES

1. Ekbom K, Ulfberg J. Restless legs syndrome. J Int Med 2009;266:419–31.
2. Allen RP, Stillman P, Myers AJ. Physician-diagnosed restless legs syndrome in a large sample of primary medical care patients in Western Europe: prevalence and characteristics. Sleep Med 2010;11:31–7.
3. Tan EK, Seah A, See SJ, Lim E, Wong MC, Koh KK. Restless legs syndrome in an Asia population: a study in Singapore. Mov Disord 2001;16:577–9.
4. Mizuno S, Miyaoka T, Inagaki T, Horiguchi J. Prevalence of restless legs syndrome in non- institutionalized Japanese elderly. Psychiatry Clin Neurosci 2005;59:461–5.
5. Ma JF, Xin XY, Liang L, et al. Restless legs syndrome in Chinese elderly people of an urban suburb in Shanghai: a community-based survey. Parkinsonism Relat Disord 2012;18:294–8.
6. Kim KW, Yoon IY, Chung S, et al. Prevalence, comorbidities and risk factors of restless legs syndrome in the Korean elderly population–results from the Korean Longitudinal Study on Health and Aging. J Sleep Res 2010;19:87–92.
7. Winkler AS, Trendafilova A, Meindl M, Kaaya J, Schmutzhard E, Kassubeck J. Restless legs syndrome in a population of Northern Tanzania: a community-based study. Mov Disord 2010;25:596–601.
8. Burtscher C, Baxmann A, Kassubek J, et al. Prevalence of restless legs syndrome in an urban population of eastern Africa (Tanzania). J Neurol Sci 2014;346:121–7.
9. Ohayon MM, O'Hara R, Vitiello MV. Epidemiology of restless legs syndrome: a synthesis of the literature. Sleep Med Rev 2012;16:283–95.
10. Innes KE, Selfe TK, Agarwal P. Prevalence of restless legs syndrome in North American and Western European populations: a systematic review. Sleep Med 2011;12:623–34.
11. Abetz L, Allen R, Follet A, et al. Evaluating the quality of life of patients with restless legs syndrome. Clin Ther 2004;26:925–35.
12. Molarius A, Kuulasmaa K, Sans S. Quality assessment of weight and height measurements in the WHO MONICA Project. WHO MONICA Project e-publications. 1998.
13. National Institutes of Health. National Heart Lung and Blood Institute, North American Association for the Study of Obesity. The practical guide: identification, evaluation, and treatment of overweight and obesity in adults. NIH Publication Number DO-4084. 2000:35–8.
14. Allen RP, Picchietti D, Hening WA, Trenkwalder C, Walters AS, Montplaisir J. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology: a report from the restless legs syndrome diagnosis and epidemiology workshop at the National Institutes of Health. Sleep Med 2003;4:101–19.
15. Popat RA, Van Den Eeden SK, Tanner CM, et al. Reliability and validity of two self-administered questionnaires for screening restless legs syndrome in population-based studies. Sleep Med 2010;11:154–60.
16. International Restless Legs Syndrome Study Group. Validation of the International Restless Legs Syndrome Study Group rating scale for restless legs syndrome. Sleep Med 2003;4:121–32
17. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989;28:193–213.
18. Ferreira KF, Eckeli A, Dach F, Schwalbach MT, Schwalbach J, Speciali JG. Prevalence of restless legs syndrome in patients with chronic pain in Maputo. Mozambique, Sleep Med 2013;14:1417–8.
19. Onwuchekwa UN, Oviasu E, Ojogwu LI, Chukwuonye II, Nnoli MA. Restless legs syndrome in End stage renal disease patients in Benin city, Nigeria. Trop J Nephrol 2011;6:107–13.
20. Celle S, Roche F, Kerleroux J, et al. Prevalence and clinical correlates of restless legs syndrome in an elderly French population: the synapse study. J Gerontol A Biol Sci Med Sci 2010;65:167–73.
21. Kim WH, Kim BS, Kim SK, et al. Restless legs syndrome in older people: a community-based study on its prevalence and association with major depressive disorder in older Korean adults. Int J Geriat Psychiatry 2012;27:565–72.
22. Giannaki CD., Hadjigeorgiou GM, Karatzaferi C, Pantzaris MC, Stefanidis I, Sakkas GK. Epidemiology, impact, and treatment options of restless legs syndrome in end-stage renal disease patients: an evidence-based review. Kidney Int 2014;85:1275–82.
23. Gigli GL, Adorati M, Dolso P, et al. Restless legs syndrome in end-stage renal disease. Sleep Med 2004;5:309–15.
24. Gemignani F, Vitetta F, Brindani F, Contini M, Negrotti A. Painful polyneuropathy associated with restless legs syndrome. Clinical features and sensory profile. Sleep Med 2013;14:79–84.
25. Li Y, Mirzaei F, O'reilly EJ, et al. Prospective study of restless legs syndrome and risk of depression in women. Am J Epidemiol 2012;176:279–88.
26. National Population Commission. Federal Republic of Nigeria, 2006 population and housing census priority table volume III; population distribution by sex, state, LGA and senatorial district. Abuja, Nigeria: National Population Commission, 2010.
27. Innes KE, Flack KL, Selfe TK, Kandati S, Agarwal P. Restless legs syndrome in an Appalachian primary care population: prevalence, demographic and lifestyle correlates, and burden. J Clin Sleep Med 2013;9:1065–75.
28. Allen RP, Walters AS, Montplaisir J, et al. Restless legs syndrome prevalence and impact: REST general population study. Arch Intern Med 2005;165:1286–92.
29. Freeman A, Pranski E, Miller RD, et al. Sleep fragmentation and motor restlessness in a Drosophila model of restless legs syndrome. Curr Biol 2012;22:1142–8.
30. Hening W, Walters AS, Allen RP, Montplaisir J, Myers A, Ferini-Strambi L. Impact, diagnosis and treatment of restless legs syndrome (RLS) in a primary care population: the REST (RLS epidemiology, symptoms, and treatment) primary care study. Sleep Med 2004;5:237–46.
31. Castriotta RJ, Murthy JN. Sleep disorders in patients with traumatic brain injury. CNS drugs 2011;25:175–85.
32. Donnemiller E, Brenneis C, Wissel J, et al. Impaired dopaminergic neurotransmission in patients with traumatic brain injury: a SPET study using 123I-β-CIT and 123I-IBZM. Eur J Nucl Med 2000;27:1410–4.
33. McAllister TW, Flashman LA, McDonald BC, et al. Dopaminergic challenge with bromocriptine one month after mild traumatic brain injury: altered working memory and BOLD response. J Neuropsychiatry Clin Neurosci 2011;23:277–86.
34. Giacino JT, Whyte J, Bagiella E, et al. Placebo-controlled trial of amantadine for severe traumatic brain injury. N Engl J Med 2012;366:819–26.
35. Kraus MF, Smith GS, Butters M, et al. Effects of the dopaminergic and NMDA receptor antagonist amantadine on cognitive function, cerebral glucose metabolism and D2 receptor availability in chronic traumatic brain injury: a study using positron emission tomography (PET). Brain Inj 2005;19:471–9.
36. Tan EK. Restless Legs Syndrome and Parkinson's Disease: is there an etiologic link? J Neurol 2006;253:VII33–7.

ACKNOWLEDGMENTS

The authors thank the research assistants whose commitment made this study a success. Author contributions: Dr. Fawale participated in the conception, organization and execution of the research project. He also participated in the design and execution of the statistical analysis and writing of the first draft of the manuscript. Dr. Ismaila participated in the conception, organization and execution of the research project. He also participated in the review and critique of the manuscript. Dr. Mustapha participated in the review and critique of the statistical analysis and review and critique of the manuscript. Dr. Komolafe participated in the review and critique of the statistical analysis and review and critique of the manuscript. Dr. Adedeji participated in the review and critique of the statistical analysis and review and critique of the manuscript.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication December, 2015
Submitted in final revised form March, 2016
Accepted for publication March, 2016

Address correspondence to: Michael B. Fawale, Neurology unit, Department of Medicine, College of Health Sciences, Obafemi Awolowo University, Ile-Ife, Nigeria; Tel: +2347065093947; Email: bimbofawale@yahoo.com

DISCLOSURE STATEMENT

This was not an industry supported study. The authors have indicated no financial conflicts of interest.