Restless Leg Syndrome in End Stage Renal Disease Patients in Benin City, Nigeria

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ABSTRACT

Restless legs syndrome (RLS) is a condition that is characterized by an irresistible urge to move one's body to stop uncomfortable or odd sensations. It most commonly affects the legs, but can also affect the arms or torso, and even phantom limbs.

Recent epidemiological studies have identified RLS as a common condition whose prevalence ranges from 3 to 10% in the general population. The frequency of RLS is higher in End Stage Renal Disease (ESRD) patients than the general population. Previous studies have shown a 6.6-83% prevalence of RLS in patients with ESRD. There is paucity of data on restless leg syndrome in Africa, prompting this study.

This is a cross-sectional descriptive study to determine the prevalence of RSL in a black African population with ESRD. One hundred and one consecutive ESRD patients were recruited; proper case histories and physical examination were conducted. Investigations performed included, Fasting blood sugar, Serum creatinine, Serum lipids, Calcium, Albumin. The Glomerular Filtration Rate (GFR) for each patient was determined using the Cockcroft-Gault equation. Structured questionnaire based on the IRLSSG diagnostic criteria was administered to all the patients.

Six patients (4 females and 2 males) from the 101 patients met the minimum criteria for diagnosis of RLS; giving a prevalence of 5.9%.

The study suggests a low prevalence of RLS in patients with ESRD in Benin City, Nigeria.

Keywords: *Restless leg syndrome; end stage renal disease; Nigerian patients.*

INTRODUCTION

Restless Legs Syndrome (RLS) is a neurologic disorder characterized by unpleasant sensation in the legs and an uncomfortable urge to move when at rest in an effort to relieve these sensations. It most commonly affects the legs, but can also affect the arms or torso, and even phantom limbs [1].

Recent epidemiological studies have identified RLS as a common condition whose prevalence ranges from 3 to 10% in the general population[2]. The most distinctive and/or unusual aspect of the condition is that lying down or trying to relax activates the symptoms. As a result, patients with restless legs syndrome have difficulty falling asleep or staying asleep. When untreated it causes exhaustion and day time fatigue. RLS is classified as either familial (primary RLS), with a clear genetic component or acquired (secondary RLS). Primary RLS occurs in approximately 50% of first degree relatives of those with RLS and is believed to be related to an inherited defect in dopamine metabolism [3]. It can be secondary to a host of conditions which include diabetes mellitus, Parkinson's disease, peripheral

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neuropathy, old age, lower income, lack of exercise and tobacco consumption [4-6].

Prevalence of RLS in ESRD ranges from 6.6-83% [7-8]. These studies were carried out in a controlled population using identical study methods. Previous studies have shown the prevalence to vary between 17-63% [9,10]. The prevalence of RLS is higher in ESRD patients than in the general population. Recent epidemiological studies have identified RLS as a common condition whose prevalence ranges from 3 to 10% in the general population [2].

The pathophysiology of RLS in uremia remains unknown, however several theories have been proposed. Potential risk factors include anemia, iron deficiency, dialysis type and duration, calcium/ phosphate imbalance, and peripheral and central nervous system abnormalities[11]. Iron is a cofactor for dopamine production in the nigrostriatal areas of the brain and iron deficiency has long been associated with the development of RLS in the general population [12,13]. In contrast, the role of anaemia and iron deficiency in the development of RLS in ureamic patients have been conflicting with only few studies indicating an inverse relationship between iron deficiency and increasing risk of developing RLS [4,14]. Treatment of RLS with high-dose iron dextran and normalization of heamatocrit with recombinant human erythropoietin have been demonstrated to improve RLS in ESRD patients [14,15]. RLS has been associated with poor quality of life, neuropsychiatric symptoms, diminished cognition, and poor attention in both ESRD patients and the general population [16-18]. Whatever the reason for increased prevalence of RLS in ESRD patients may be, studies have shown that the condition can be cured or ameliorated after a successful renal transplantation in some cases[12].

Currently, there is no single diagnostic test for RLS. The disorder is diagnosed clinically, by evaluating the patient's history and symptoms. In 1995, the International Restless Legs Syndrome Study Group (IRLSSG) Identified four basic criteria for diagnosing RLS [19]. IRLSSG also developed a rating scale for evaluating wide range of symptom severity in RLS patients [20]. The IRLSSG diagnostic criteria were used in this study.

There is paucity of data on restless leg syndrome from Africa[8, 21], and the present study therefore aims at determining the prevalence of this condition amongst Nigerian patients in ESRD and evaluating possible contributory factors to such level of prevalence.

MATERIALS AND METHODS

This is a cross sectional descriptive hospital based study carried out on patients being managed for ESRD in University of Benin Teaching Hospital, and Central Hospital Benin City, Nigeria. The study was carried out over a 13 month period. Consecutive patients attending the renal clinics were recruited, subject to satisfying the inclusion criteria. A total of 101 of ESRD patients were recruited for the study. The test procedure was explained to all the subjects

Inclusion Criteria

(i)Patient confirmed to have ESRD based on history, physical examination, biochemical and Radiological investigations.

(ii) Patients chosen were of age 18 years and above.

Exclusion Criteria

(i) Patients who were below 18 years of age

(ii) Patients who refused to give consent

Ethics

Ethical clearance was obtained from the ethical committee of the hospital and informed consent was also sought and obtained from all the study subjects.

Data Collection

A data acquisition form was used to collect information from medical history and physical examination of all the study subjects, including relevant socio – demographic data.

Blood pressure (BP) was measured with mercury sphygmomanometer using the standard methods. Systemic hypertension was defined as systolic BP greater than or equal to 140mmHg and or diastolic BP greater than or equal to 90mmHg [22].

Investigations

Investigations performed included serum Electrolytes, Urea and Creatinine, Albumin, calcium, fasting lipid profile, Fasting Blood Sugar (FBS), and Packed Cell

Volume (PCV). The GFR of each patient was also estimated using the Cockroft-Gault equation.

Essential Diagnostic Criteria for RLS (IRLSSG)

(a) A desire to move the extremities, often associated with paresthesias/dysesthesias;

(b) Motor restlessness

(c) Worsening of symptoms at rest with at least temporary relief by activity, and

(d) Worsening of symptoms in the evening or night.

(e) Other features commonly seen in RLS include sleep disturbance, periodic limb movements in sleep and similar involuntary movements while awake, a normal neurological examination in the idiopathic form, a tendency for the symptoms to be worse in middle to older age, and, in some cases, a family history suggestive of an autosomal dominant mode of inheritance [19, 20].

GFR determination

The GFR was estimated using the Cockroft and Gault predictive formula:

$$GFR = \frac{\{140 - Age(years)\} \times weight\ (kg) \times 88}{72 \times Serum\ Creatinine\ (\mu mol/l)}$$

Multiply by 0.85 if female

This formula is still one of the best predictive formulae in our setting, because of the ease of its recall and high correlation coefficient of determination in both health and disease state[23]

Data Analysis

Data from the study were analyzed using the statistical Package for Social Sciences (SPSS) version 3.1. The probability values were calculated using prevalence of RLS amongst ESRD patients and divided by the total number of ESRD patients. Scores were standardized with z- scores for determination of relative frequencies. Correlation analysis of some metabolic variables of ESRD patients with RLS was computed using Pearson correlation coefficients.

The relationship between RLS and some sociodemographic variables, like fasting blood sugar, Body Mass Index (BMI), Packed Cell Volume (PCV), and Fasting Lipid Profile among ESRD patients was also explored with Pearson correlation coefficient. The differences between mean age, height, weight, BMI and educational status were statistically analyzed using a multivariate analysis of Variance (ANOVA). Tests of hypotheses were computed using inferential statistics to determine whether there is statistical difference (Pd"0.05) between ESRD patients with and without RLS in the sample statistics.

RESULTS

In all, a total of 101 patients took part in the study. Fifty four (53.5%) of the patients were males, while 47 (46.5%) were females. Assessing the educational qualification of the patients, 13.86% had no formal education, 30.69% had only primary education, 28.71% ended their formal education after secondary school, while 26.73% attended tertiary institutions. Patients in the age range of 20-30years constituted 28.7%; those in the range of 40-59years constituted 45.5% and those above 60years made up the remaining 24.8%. The mean age of the males in the study was 49.8±15.2yrs, while that of the females was 45.2±16.2yrs. The mean age of both males and females with ESRD only was 47. 81±15.54, while the mean age for ESRD with RLS was 45.17±20.37. Fifty five of the patients had normal BMI (54.5%), 24 (23.8%) were overweight, 15(14.9%) obese and only 7(6.9%) were underweight, using the WHO classification. The mean BMI for all the patients was 24.6±4.7, while the mean for only those with RLS was 25.82±6.96.

Table 1: Relationship between sex and RLS

Gender	ESRD only	ESRD + RLS	Total
Male	52(54.7%)	2(33.3%)	54(53.5%)
Female	43(45. 3%)	4(66.7%)	47(46.5%)
Total	95(100%)	6(100%)	101(100%)

X^2 (with Yates correction) = 0.357, p = 0.550 not significant.

Only 6 (5.94%) of the 101 patients recruited for the study were found to meet the minimum criteria for RLS set by IRLSSG. One of the patients with

Table 2: Relationship between RLS and BMI

BMI	ESRD ONLY	ESRD WITH RLS	TOTAL
UNDERWEIGHT	5(5.3%)	2(33.3%)	7(6.7%)
NORMAL	54(56.8%)	1(6.7%)	55(54.5%)
OVERWEIGHT	23(24.2%)	1(6.7%)	24(23.8%)
OBESE	13(13.7%)	2(33.3%)	15(14.9%)
TOTAL	95(100%)	6(100%)	101(100%)

Fisher exact test = 8.069, p = 0.021 significant.

Table 3: Relationship between RLS and renal function test and PCV

Parameters	ESRD	Mean	Std. Deviation	T and P values
Serum creatinine	ESRD only	832.50	489.30	t =0.149
(ìmol/l)	ESRD+RLS	672.3	216.5	p = 0.419
Urea(mmol/l)	ESRD only	61.60	29.05	t = 1.014
	ESRD+RLS	208.50	73.07	p = 0.313
GFR(ml/min)	ESRD only	13.13	10.89	t = 1.339
	ESRD + RLS	2.30	1.98	p = 0.217
PCV (%)	ESRD only	23.63	7.03	t = 0.951
	ESRD + RLS	20.83	5.53	p=0.951

Table 4: Relationship between RLS and biochemical parameters

Parameters	ESRD	Mean	Std. Deviation	t and p values
Cholesterol	ESRD only	5.21	1.93	t =0.687
(mmol/l)	ESRD + RLS	5.76	1.70	p=0.493
Triglyceride	ESRD only	1.66	0.79	t=1.272
(mmol/l)	ESRD + RLS	2.08	0.84	p=0.206
Calcium (mmol/l)	ESRD only	1.86	0.10	t=2.103
	ESRD + RLS	1.71	0.14	p=0.062
Albumin (g/l)	ESRD only	34.0	7.4	t=0.857
	ESRD + RLS	31.3	4.2	p=0.393
RBS (mmol/l)	ESRD only	5.45	1.44	t=0.067
	ESRD + RLS	5.49	1.59	p=0.947

RLS was within the age range of 20-29years, another was within the age range of 30-39years, 3 were within the age range of 40-49years while 1 was above 80years. It was found that neither the age groups nor the mean ages, of the respondents were significantly related to the occurrence of RLS (fishers exact test =8.443, P-0.236 and t-0.397).

Table 3 depicts the relationship between RLS and renal function (urea, creatinine and GFR) and also PCV. There was no statistical difference in the mean value of each of the above parameters with or without RLS.

Table 4 compared the mean values of some biochemical parameters. None of the biochemical parameters was found to significantly vary with the occurrence of RLS in ESRD, when compared using the student t-test.

DISCUSSSION

Restless Legs Syndrome, a sensorimotor disorder with a profound impact on sleep has been called the "most common disorder that you have never heard of". Although studies have shown that it has a prevalence of 3-10% in the general population, many physicians are not very familiar with it, thus adversely affecting the quality of care received by such patients.

A total of 6 (5.9%) people from our study population had RLS. This prevalence is low when compared with figures from other studies (6.6-83%) [7-10, 24]. The results suggest that the prevalence of RLS may be lower in blacks, and this is in agreement with the study carried out by Chaudhuri *et al* [25] in which he showed a low prevalence amongst Africans and Asians (0.1 to 5%).

The mean age of ESRD patients with and without RLS was 45.17±20.40 and 47.80±15.5. This result shows that most patients with ESRD in Nigeria are young adults; this is in agreement with an earlier study by Salako *et al* [26]. Over 60% of the patients in this study were young adults. The young adults usually constitute the working age group that should be the breadwinners of their families. The mean age of those ESRD patients with RLS was 45.17±20.4years. In more developed countries of the world, ESRD is usually more common among the elderly. Gilgi reported that the average age of his patients with RLS was 65years, and that 82% of the ESRD patients with RLS were over 45years. Primary RLS appears to increase with age, but RLS in ESRD patients in this study did not show that pattern. Although the prevalence of primary RLS appears to increase with age, it has a variable age of onset, and can occur in children [27]. The sociodemographic parameters of ESRD patients when compared with those with ESRD plus RLS were similar. In this study more women had RLS than men, a total of four women had, while only two men had the condition. This tends to suggest that RLS is more common in women than in men. This is in agreement with an earlier study by Berger [28] but some other studies do not agree with this [12, 24]. It may be that female preponderance is related to serum iron level. Females generally have lower iron status than males. 0'Keeffee and colleagues [29] found a correlation between serum ferritin levels and the severity of RLS in the elderly. Further evidence of the relationship between iron deficiency and RLS could be found in the three major secondary causes of RLS which include, ESRD, pregnancy and iron deficiency anaemia-all of which involve low levels of serum iron [30].

The mean serum calcium, albumin, and FBS of ESRD patients, with and without RLS did not show any significant difference. Also, the mean systolic and diastolic blood pressures of both groups did not show statistically significant difference. No sociodemographic or biochemical determinants of RLS in ESRD patients were found in this study; in addition, the PCV did not vary significantly between those patients with ESRD only, and those with ESRD plus RLS.

From the present study, the observed low prevalence of RLS among our ESRD patients may be a reflection of the very low prevalence of the disorder earlier reported in a normal African population[25]. This may however need to be confirmed by a much larger prospective study.

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