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IMPACT OF PERIPHERAL NEUROPATHY ON GAIT AND FREQUENCY FALLS IN PEOPLE LIVING WITH HIV

***Nweke, M.C.[1], Ezema, C.I.[1], Idika M.[1]**
[1]Department of Medical Rehabilitation, Faculty of Health Sciences and Technology University of Nigeria Enugu Campus, Enugu Nigeria.
* Corresponding author: E-mail:martins.nweke@gmail.com

ABSTACT

This study evaluated the impact of HIV induced Peripheral neuropathy (HIV-PN) on gait parameters and frequency of falls among 69 patients (25males, 44 females).A convenient sampling technique was employed. Participants were screened of PN using the HIV-brief PN tool, which comprises tests of subjective symptom, vibration sense and reflex. Vibration perception was examined using 128Hz tuning fork, and ankle reflex was examined with the aid of tendon hammer, in supine position. Measurement and analysis of gait parameters were done with the aid of 10-meter walking test and an invented comparative velocity field diagram respectively. Results showed that 45(65%) of the participants had PN of mild to moderate degree. The PN differed significantly one from another in gait speed ($P<0.05$), step length ($P<0.05$), stride lengths ($P<0.05$) and stride velocity ($P<0.05$), irrespective of the walking pace. At fast walking pace, however, participants with mild or moderate PN differed significantly from those without PN in terms of cadence ($P<0.05$) and stride frequency ($P<0.05$). Having moderate loss of vibration sense or subjective symptom grade 2 increased the odd of fall by 10% (P=0.048, OR=0.1) and 80% (P=0.004, 0.8) respectively. PN predisposes to gait deficits, and falls especially as walking pace increases.

Key words: HIV infection, neuropathy, gait, falls, comparative velocity field diagram

INTRODUCTION

Peripheral neuropathy (PN) is one of the most common neurological complications of Human Immune Virus (HIV) .infection (Nwabueze *et al*., 2013, Keswania *et al*., 2012). It is common at all stages of human immunodeficiency virus infection and causes considerable morbidity with symptoms like 'aching', 'painful numbness', or 'burning' sensation (Keswania *et al*., 2012). Its symptoms are usually most severe on the soles of the feet, and are typically worse at night (Keswania *et al*., 2012). Before the introduction of the pre-Highly Active Antiretroviral Therapy (HAART) in 1995, global estimate of prevalence of HIV-Sensory Neuropathy (HIV-SN) among patients with Acquired Immune Deficiency Syndrome (AIDS) was 35% (Schifitto *et al*., 2001).

However, in the post-HAART era, the prevalence of HIV-SN has increased to between 50% and 60% (Luma *et al*., 2012; Maritz *et al*., 2010). This increase has been attributed partly to the use of HAART and partly to the different definitions of HIV-SN (Robinson-Papp *et al*., 2012). Some studies defined HIV-SN as one clinical sign (e.g. reduced ankle reflexes or reduced pinprick sensation or reduced vibration sensation in the feet), while some required two clinical signs, and others used validated screening or diagnostic instruments (Robinson-Papp *et al*., 2012; Anziska *et al*., 2012).

In Africa, prevalence of HIV-SN has been reported (Parry *et al*., 1997; David *et al*., 2014). In Nigeria, prevalence of HIV-SN has been reported to be 38% or 39% (Osinaike *et al*., 2012; Anastasi *et al*. 2013). HIV-PN alters peripheral functioning and it's characterized by symptoms like 'aching', 'painful numbness', or 'burning' sensation and Achilles' tendon reflex (Keswania *et al*., 2012). These alterations in peripheral functioning may result in concomitant alteration in gait leading to loss of balance, difficulty walking, limited physical activity and falls (Studenski *et al*., 2011).

Gait is a complex brain process that involves the integration of motor, sensory, and cognitive processes, including memory, attention, and executive functions (Watson *et al*., 2010). It is a strong indicator of health, and poor gait is associated with higher mortality, morbidity, and risk of falls (Maki1997; Nakamura *et*

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al., 1997; Rapp *et al*., 2012). Gait parameters represent predictive indicators of fall-risk in people with balance problem (Latash, 2008). Gait deficits are among the leading risk factors for falls in both community dwelling and institutionalized older adults. These deficits may result in difficulty crossing a street, incontinence accidents, or cause people to rush more than usual and may further escalate their instability and risk of falling (Stuart and Rose, 1998). Even mild deficit in parameters of gait affects functional mobility. For example, reduction in walking speed impedes one's ability to navigate between two points in a timely manner (Stuart, & Rose 1998).

The capability to execute walking efficiently either as an essential activity of daily living, prescribed therapy or skilled occupation is based, in part, on intact cognition, one's perceived self-efficacy and efficient biofeedback (Stuart and Rose, 1998; Manning *et al*., 1997; Deborah *et al*., 2005). This suggests that gait is polygenically determined by interplay of network of forces ranging from neuronal to psychosocial mechanisms (Harischandra *et al*., 2015). Neuronally, much credence has been attributed to the central patterns as sole determinant of gait pattern with little or no regards to the role of sensory input (Stuart and Rose 1998).

The role of peripheral inputs during walking activity is not completely understood (Guertin *et al*., 1995), however, it is not doubtful, in non-pathological cases, that the control system requires those sensory inputs for successful and efficient progressions during locomotion (Guertin *et al*., 1995; Pearson 1995; Gordon *et al*., 2008). Intact sensory integrity plays important role in walking, though its part must be regulative not causative (Guertin *et al*., 1995; Pearson, 1995). Basically, the roles of sensory inputs include modulating and adapting central pattern to environmental constraints or obstacles, reinforcement in generation of muscle torque etc. (Gordon *et al*., 2008). For instance, small fibre neuropathy which is characterized by pain, paraesthesia/numbness results in insufficient joint torque and ground reaction force leading to antalgic gait and slapping gait abnormalities respectively (Nordqvist, 2015). Also, large fibre neuropathy characterized by reduced joint proprioception should result in sensory ataxia and consequent postural instability, stamping gait and increased risk for fall (Erlandson *et al*., 2012). Although PN causes loss of protective function and puts patients at elevated risk for foot injury and falls, gait assessment and foot care for people with HIV/AIDS is often overlooked (Studenski *et al*., 2011;Krucik, 2013). This could be attributed to scanty research regarding the impact of HIV-PN on gait and frequency of falls. The study was therefore designed to evaluate the impact of HIV-PN on gait parameters and frequency of falls.

MATERIALS AND METHODS

Study Area: The study took place in University of Nigeria Teaching Hospital and Enugu State University Teaching Hospital, Enugu.

Participants' description: HIV-seropositive individuals who attended the PEPFAR HIV clinics of the above mentioned teaching hospitals.

Sample procedure: A convenient sampling technique was employed in this study.

Sample size: Considering the degree of freedom for a three groups (df) (nil neuropathy, mild neuropathy, moderate neuropathy), from cohen table, a post-study power analysis showed that to detect an effect size of 1.0, at a power (β) of 0.9 and 0.05 level of significance, a minimum sample of 66 subjects would be required (Cohen 1988). However, a total of 69 HIV-seropositive individuals were recruited into the study.

Inclusion criteria: The inclusion criteria included being HIV seropositive, between ages 18-65yrs, and being able to walk distance of 10meters independently with or without support.

Exclusion criteria: The following constituted criteria for exclusion in the study- being older than 65 years, having severe osteoarthritis of the lower limb joints as defined by Krucik (Simpson et al. 2006), recent head injury, psychosis, hearing loss and/or recent soft tissue injury. Informed consent was sought and obtained from each participant.

Participants of the study: HIV seropositive individuals with or without peripheral neuropathy who were capable of independent ambulation with or without support. Participants' socio-demographic and anthropometric characteristics such as sex, age,

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marital status, presence of joint pain of mild to moderate degree, history of fall, years since HIV and duration on HAART were collected. Ethical clearance was obtained from the Research Ethical Review Committee, University of Nigeria Teaching Hospital, Enugu.

Assessment of HIV-PN: HIV-PN was assessed using the brief PN tool (BPNST). This is a validated tool used in screening for PN. It provides a quick and easy assessment of neuropathy at the bedside and does not require neurophysiologic testing. It has sensitivity and specificity range of 35%–49% and 88%–90% respectively, with a positive predictive value of 72% (Ellis *et al*., 2005; Cherry *et al*., 2005). The BPNST assesses subjective symptoms and objective signs of PN. The BPNST rates presence and severity of subjective symptoms for each leg separately, using a scale of 1(mild) to 10 (severe), including pain, aching, or burning in feet and/or legs, pins and needles in feet and/or leg, and numbness in feet and/or legs. Secondarily, the objective signs were assessed using 128Hz tuning fork and reflex hammer and scored as follows. In scoring subjective symptoms: The highest of the six scores (3 for each leg) was converted to a subjective PN grade as follows: symptoms absent (grade 0), score 1-3 (grade 1), score of 4-6 (grade 2) and score of 7-10(grade 3) (Mehta *et al*., 2011).

Diagnostic Criteria for HIV-PN: In this study, PN was diagnosed as presence of at least two of the distally predominant PN signs. This is in line with (Anziska *et al*., 2012; Devigili *et al*., 2008; Jan-Willem *et al*. 2005). These signs include pain, aching or burning, pins and needle, diminished reflex, and altered sensation. Small fibre PN is diagnosed by the presence of at least two of these symptoms: pain, aching or burning in feet/legs, pins and needles in feet/legs and numbness (lack of feeling) in feet/legs (Anziska *et al.,* 2012), while large fibre PN is diagnosed by the presence of at least two of the symptoms of loss of joint position sense, reduced or absent deep tendon reflex, insensibility to light touch and loss of vibration sense (Devigili *et al*., 2008; Jan-Willem *et al*., 2005).

Assessment of vibration perception: The 128Hz Gardiner Brown medical tuning fork is designed for diagnosing sensory/PN by testing for vibration perception. Tuning fork vibration sense was defined as normal for a vibration felt for more than 10 seconds, mild loss for 6-10 seconds and moderate loss for ≤5 seconds and severe loss for no feeling of vibration. It has accuracy of 78.9%. Use of the 128-Hz tuning fork is a valid and reliable test for screening purposes and manageable in clinical practice.

The accuracy, sensitivity and specificity of vibration testing for PN have been estimated to be 78.9, 53 and 99 percent respectively (Jayaprakash *et al*., 2011)**.** Vibration perception was scored following Jan-Willem et al. (Jayaprakash *et al*., 2011), with score of 0 = felt >10 seconds (normal), 1 = felt 6-10 seconds (mild loss), 2 = felt <5 seconds (moderate loss), 3 = not felt (severe loss) and 8 = unable to or did not assess. In this study, participants were made to sit in a chair facing the seated examiner, and with their foot wear removed. The examiner lifted each participant's foot to rest on his lap using his left hand. Using the right hand, the 128Hz turning fork was maximally struck on wooden object and applied to the distal interphalangeal joint of the hallux of the participants' foot. Participant was earlier asked to say 'STOP' when he/she does not feel the vibration any longer. The duration for which vibration was felt was recorded using a stop watch. Vibration sense was defined as normal for a vibration felt for more than 10 seconds, mild loss for 6-10 seconds and moderate loss for ≤5 seconds and severe loss for no feeling of vibration.

Assessment of Achilles tendon reflex: This was used to assess the integrity of participant's ankle reflex. Ankle reflexes will be defined as absent, hypoactive, normal and hyperactive or clonus. The inter-rater reliability analysis showed a high correlation between examiners for deep tendon reflex using reflex hammer (ICCs 0.91–0.96) (Yong-wok, 2015).Scoring:0= absent; 1= hypoactive; 2= normal reflex response; 3= hyperactive; 4= clonus; 5= unable to or did not assess. Participants were asked to assume high sitting position in a couch with the ankle relaxed. The ball of the foot was supported by putting some tension in Achilles tendon without completely dorsiflexing the ankle using the examiner's left hand. The Achilles tendon was gently struck to elicit jerk-like response. Whenever no response was obtained, participant was asked to clench his/her fist with the ankle reflex then retested before classifying reflex as absent. Total absence of ankle reflex with reinforcement was regarded as an abnormal result.

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Measurement and Analysis of Gait parameters: The 10 m walk test (10mWT) was the tool used to evaluate the spatial, temporal, and kinematic attributes of gait (Markides, 2001). It is one of the widely method of evaluation of mobility and gait pathology. Internal consistency (ICC) of timed walking tests (time measured with a stopwatch, step count for the 10MWT) ranged from 0.89–0.97 (Novaes1 et al. 2011). ICCs of temporo-spatial gait parameters ranged from 0.81–0.95 (10MWTprefered) and from 0.61–0.90 (10MWTmax) (Graser *et al*., 2016). To eliminate the acceleration and deceleration components, the volunteers were instructed to begin walking 2m before the beginning of the course and to finish 2m after the end of the course at usual speed. Two tests were carried out to minimize learning effect, and the average was used for data analysis. Walking speed in meters/second was obtained by dividing the timed sequence by the elapsed time. A single examiner using a stopwatch recorded the walking time of all participants and registered the number of steps and strides taken during the course. The number of steps taken during the timed sequence by the elapsed time was counted, and cadence was calculated as number of steps divided by the elapsed time. The participants were asked to repeat the procedure at slow walking speed (velotype 2) and fast walking speed (velotype 3). For each participant, at different walking speed, gait parameters were calculated as follows: Stride= [2*number of step], stride length, λ= [distance/number of stride], stride duration= [time taken/number of stride], stride frequency, *f*= [1/stride duration] and stride velocity= [$f\lambda$].

A summary regression plot, the comparative field diagram was invented to evaluate interaction of gait parameters, and compare such interaction between fallers and non-fallers first, and then among participants groups: nil PN, mild and moderate PN. It is a plot of stride length, stride velocity and stride frequency against velotype (walking pace category). In this study, the comparative velocity field diagram was used to further elucidate the likelihood of fall in participants with HIV-PN. Velocity field diagram has been used by Eke-Okoro (1989) to predict falls in community dwelling older adults. The difference between the former and the later is that the former, the comparative field diagram comprises two independent but summative plots. The first plot (fallers versus non-fallers) provides a yardstick for the interpretation of 2nd plot, which provides comparative gait analysis among the disease groups namely Nil PN, mild and moderate PN. This means that plot 2 was interpreted with plot 1 in view. Though its validity and reliability in predicting of fall in disease conditions is yet to be tested, its result, to a large extent, is consistent with those obtained by analysis of variance and independent sample t-test.

Data Analysis: Data analysis was done using the Statistical Package for Social Sciences (SPSS) version 22. Descriptive statistics was used to summarize the socio-demographic characteristics, occurrence of PN and self-reported history of fall. Chi square test was used to test for difference in proportion of occurrence of fall among participants with nil PN, mild PN and moderate PN. One-way Analysis of Variance was used to test for differences in gait parameters among HIV-seropositive persons with no PN, mild PN and moderate PN. Independent sample t-test was used to compare gait outputs of fallers and non-fallers. Gait analysis was aided with use of comparative velocity field diagram. Hierarchical regression was used to examine the impact of PN on frequency of falls in PLWH.

RESULTS

A total of 69 (25males, 44 females) HIV-seropositive individuals participated in this study. More than half (75%) of the participants were ≤50 years. The modal age class was ≤30years (39.1%). Seventeen (24.6%) of the participants reported an experience of fall. Forty two (60%) participants have had HIV within 5years ago, 20 (29%) have had the virus for period between 6-10years, while 2 (2.9%) have had the virus for more than 10years. More than half (56.5%) of the participants have been on HAART for period between 1-5years, 20 (29%) have been on HAART for 6-10years while 2 (2.9%) have been on HAART for period >10years. Approximately one-fifth of the participants had experience fall since the last visit to clinic (Table 1).

Forty-one (59%) of the participants had sensory neuropathy (pain, aching, burning, pins and needle, and/or numbness. Of this, mild neuropathy and moderate neuropathy numbered 18(26.1%) and 23(33.3%) respectively. Approximately 48% of the participants had impaired vibration sense of mild to moderate degree. The prevalence of dysreflexia was 46.4%, with hyporeflexia (hypoactive) and areflexia

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(absent) numbering 30(37.7%) and 13(8.7%) respectively. Overall, 45(65%) of the participants had PN of mild to moderate degree (Table 2A and 2B). Cross-examination of the factors associated PN in HIV-seropositive individuals reveals age as the most important factor (X^2 =59.536, P<0.05), followed by years since HIV (X^2=38.438, P<0.05), duration of HAART (X^2=35.457, P<0.05), diabetes (X^2=17.853, P<0.05) and sex (X2=17.85, P<0.05).

Table 1: Socio-demographic and clinical characteristics of participants

Characteristics	Frequency	Percent (%)
Age (yrs)		
≤30	27	39.1
31-40	15	21.7
41-50	12	17.4
51-60	11	15.9
>60	4	5.8
Sex		
Male	25	36.2
Female	44	63.8
Duration of illness (yrs)		
0-5	42	60.9
6-10	20	29.0
11-15	5	7.2
Missing	2	2.9
Duration of HAART (yrs)		
<1	6	8.7
1-5	39	56.5
6-10	20	29.0
>10	2	2.9
Missing	2	2.9
Self-reported history of fall		
Fallers	17	24.6
Non-fallers	52	75.4

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Table 2A: Distribution of participants based on PN status using the brief PN tool, and Factors associated with peripheral HIV-neuropathy

Domain	Frequency	Percent
Symptoms		
Nil	28	40.6
Mild sensory neuropathy	18	26.1
Moderate sensory neuropathy	23	33.3
Severe sensory neuropathy	-	-
Vibration perception		
Normal	36	52.5
Mild loss	22	31.9
Moderate loss	11	15.9
Severe loss	-	-
Achilles' tendon reflex		
Normal	37	53.6
Hypoactive	26	37.7
Absent	6	8.7
Overall PN status		
Nil	23	33.
Mild	21	304
Moderate	24	34.8
Missing	1	1.4

Table 2B: Factors associated with fall in their other of importance

	PN status				
Age (years)	Nil PN	Mild PN	Moderate PN	X^2	*P*
≤30	22	4	1	59.536	0.000*
31-40	4	9	2		
41-50	-	1	11		
51-60	-	3	8		
>60	-	2	2		
Years since HIV(years)					
≤5	26	13	3	38.438	0.000*
6-10	-	5	15		
11-15	-	1	4		
HAART duration(years)					
<1	5	1	-	35.457	0.000*
1-5	21	13	5		
6-10	-	5	15		
>10	-	-	2		
Diabetes					
Yes	2	3	14	17.853	0.000*
No	24	16	10		
Sex					
Male	13	8	4		
Female	13	11	20	6.393	0.041

Analysis of variance shows, at regular walking speed, significant differences in step and stride length among participants with nil PN, mild PN, and moderate PN ($P<0.05$), with each group differing significantly one from another ($P< 0.05$) except for stride velocity where participants with mild PN and moderate PN did not differ from each other significantly ($P>0.05$). Analysis of variance shows, at slow walking speed, significant differences in walking speed, step length and stride length among participants with nil PN, mild PN and moderate PN ($p<0.05$), with each group differing significantly from one another ($P<0.05$). In velotype 3, significance differences ($P<0.05$) were found in all parameters of gait except for step and stride durations ($P>0.05$). Regarding walking speed, step and stride lengths, each of the participants groups differed significantly from each other ($P<0.05$), while differences in cadence, stride frequency and stride velocity were found only between nil PN group and each of mild PN and moderate PN ($P<0.05$) (Table 4).

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Analysis of variance reveals, at regular and slow walking speed, significant differences in walking speed, step length, stride length, stride length and stride velocity between fallers and non-fallers, with fallers exhibiting slow walking speed and stride velocity, short step and stride length (P< 0.05). At fast walking pace, similar result was obtained in addition to significant difference in cadence and stride frequency (P< 0.05).

Table 4: Comparison of gait parameters between fallers and non-fallers

Parameter	Fallers Mean±SD	Non-fallers Mean±SD	t	*P*
SLOW				
Cadence	58.86±14.28	54.56±8.41	1.172	0.246
Walking speed	0.79±0.17	0.65±0.07	3.365	0.001*
Step length	0.84±0.21	0.72±0.12	2.182	0.033*
Stride length	1.64±0.40	1.33±6.31	2.950	0.004*
Step duration	1.07±0.24	1.13±0.19	-0.795	0.430
Stride duration	2.15±0.48	2.25±0.36	-0.763	0.448
Stride frequency	0.49±0.122	0.45±0.087	1.282	0.204
Stride velocity	0.78±0.18	0.58±0.16	3.943	0.000*
REGULAR				
Cadence	68.11±12.47	61.34±11.81	1.969	0.053
Walking	1.17±0.39	0.86±0.19	3.100	0.003*
Step length	1.05±0.30	0.85±0.11	2.639	0.010*
Stride length	2.10±0.61	1.75±0.34	2.639	0.030*
Step duration	0.92±0.22	1.02±0.21	2.212	0.097
Stride duration	1.84±0.45	2.04±0.42	-1.682	0.106
Stride frequency	0.57±0.11	0.51±0.10	-1.640	0.071
Stride velocity	1.18±0.37	0.89±0.23	1.832	0.005*
FAST				
Cadence	76.16±18.0	63.14±16.45	2.643	0.010*
Walking	1.46±0.58	1.01±0.29	3.069	0.003*
Step length	1.12±0.53	0.98±0.18	1.675	0.999
Stride length	2.19±0.65	1.96±0.36	1.362	0.178
Step duration	0.84±0.21	1.01±0.29	-2.720	0.008*
Stride duration	1.67±0.42	2.02±0.58	-2.725	0.008*
Stride frequency	0.64±0.15	0.52±0.13	2.962	0.004*
Stride velocity	1.40±0.55	1.01±0.27	2.766	0.007*

*: significant at α=0.05

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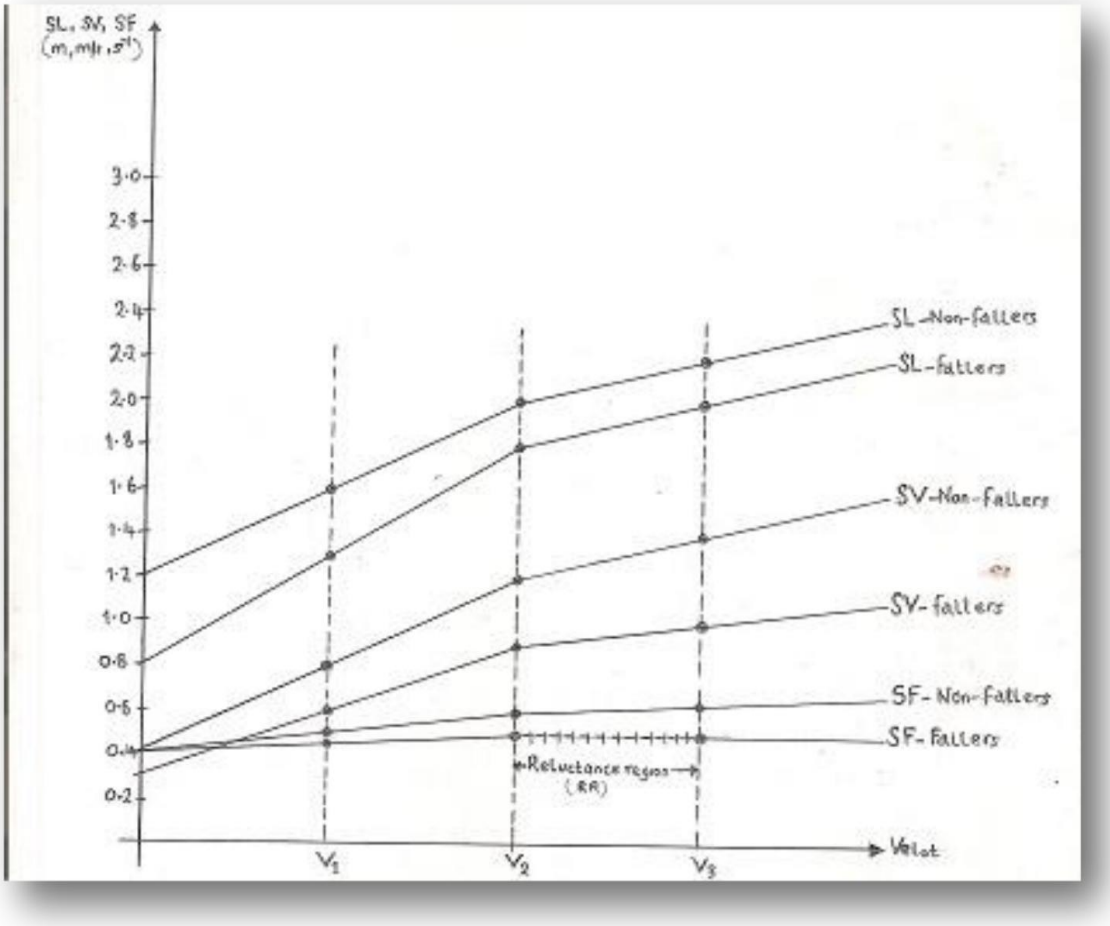
The regression plot shows comparative and summative analysis of gait parameters between fallers and non-fallers. In terms of stride length and velocity, both fallers and non-fallers showed stable transition moving from velotype 1 to velotype 3. The actual difference between fallers and non-fallers was found in stride frequency; while non-fallers showed stable change in stride frequency with increasing walking speed, fallers showed constant (reluctance to change in) stride frequency as walking speed increases from velotype 2 to 3 (Figure 1). In this figure, reluctance region (RR) is marked by dotted lines (brakes) to show unwillingness to accelerate by improving stride frequency .



RR=reluctance region; SL=stride length; SV=stride velocity; SF=stride frequency; PN=peripheral neuropathy

Figure 1: Regression plot 1 showing comparative and summative analysis of gait parameters between fallers and non-fallers

Comparative examination of the interaction of gait parameters among participants with no PN, mild and moderate PN shows a similar and consistent increase in stride length throughout the velotypes. However, moving from V2 to V3, participants with mild PN had challenge altering their stride length. Regarding stride velocity, participants with no PN or mild neuropathy show stable transition in stride velocity at varying walking speeds, while those with moderate PN exhibited constant (reluctance to change in) stride

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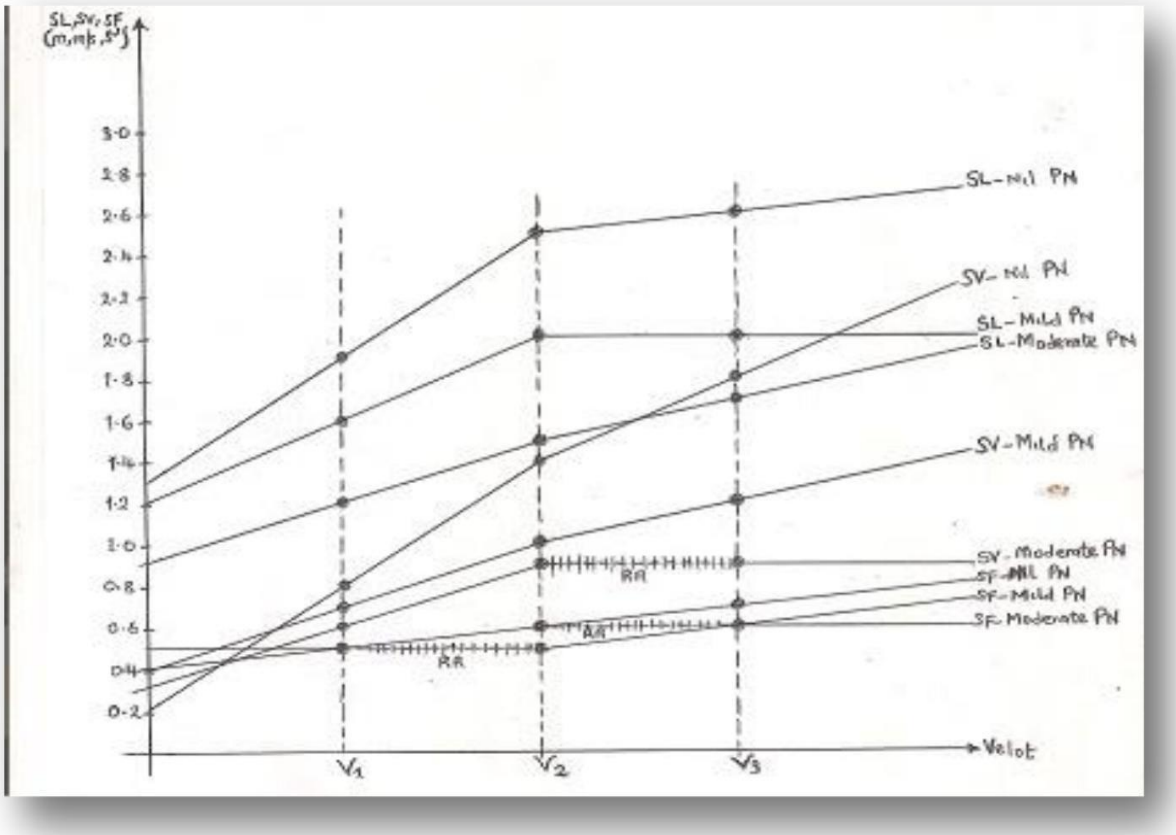
velocity from velotype 2 to 3. In terms of stride frequency, participants with mild or moderate PN showed constant stride frequency at different points. For participants with mild PN, difficulty with changing stride frequency occurred when moving from velotype 1 to velotype 2, while participants with moderate PN had similar challenge moving from velotype 2 to velotype 3. Reluctance region is marked by dotted lines to show unwillingness to accelerate or decelerate beyond preferred walking pace (Figure 2).



RR=reluctance region; SL=stride length; SV=stride velocity; SF=stride frequency; PN=peripheral neuropathy

Figure 2: The regression plot shows comparative and summative analysis of gait parameters among participants with nil PN, mild PN and moderate PN

Logistic **re**gression shows vibration perception and subjective symptoms to be independent predictors of fall in people living with HIV-PN; having moderate loss of vibration sense and subjective symptom grade 2 (moderate sensory neuropathy) increased the odd of experience fall by 0.1 (P=0.048, OR=0.1) and 0.8 respectively (P=0.006, Δ-2-loglikelihood=11.183, OR =0.8) (Table 7).

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Table 7:Stepwise forward logistic regression showing degree of contribution of various components of PN to falls

	P	OR (%)
Step 1		
Intact vibration sense¶		
Mild loss	0.004	0.038
Moderate loss	0.048	0.1
Step 2		
Nil subjective symptom¶		
Subjective symptom grade 1	0.998	0.000
Subjective symptom grade 2	1.000	1.000
Intact vibration sense¶		
Mild loss	0.269	0.2
Moderate loss	0.048	0.1
Step 3		
Nil subjective symptom¶		
Subjective symptom grade 1	0.998	0.000
Subjective symptom grade 2	0.891	0.889

		model log likelihood	Δ-2-log likelihood	P
Step 1	Vibration	-21.254	9.646	0.008
Step 2	Vibration	-16.431	6.034	0.048
	Subjective	-15.662	4.497	0.106
Step 3	Subjective	-21.254	11.183	0.004

¶: reference category.

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Parameter	Nil PN	Mild PN	Moderate PN	Total		
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	F	*P*
SLOW						
Cadence(steps/min)	54.47±12.67[a]	55.40+7.49[a]	62.48±16.15[a]	57.88±13.13	2.74	0.072
Walking speed (m/s)	0.89±0.16[a]	0.72±0.13[b]	0.64±0.05[c]	0.75±0.16	25.61	0.000*
Step length (m)	0.98±0.11[a]	0.78±0.14[b]	0.65±0.17[c]	0.81±0.19	33.86	0.000*
Stride length (m)	1.88±0.24[a]	1.56±0.28[b]	1.23±0.35[c]	1.56±0.40	31.77	0.000*
Step duration (s)	1.45±0.27[a]	1.33±0.26[a]	1.21±0.26[a]	1.33±0.28	5.32	0.007*
Stride duration(s)	2.31±0.49[a]	2.21±0.32[a]	2.02±0.49[a]	2.18± 0.45	2.41	0.098
Stride frequency	0.45±0.11[a]	0.47±0.06[a]	0.52±14[a]	0.48± 0.12	2.28	0.110
Stride velocity(m/s)	0.84±0.19[a]	0.74±0.16[a]	0.60±13[b]	0.73±0.19	12.76	0.000*
REGULAR						
Cadence	67.88 ±12.86[a]	63.46±12.61	67.75±12.60[a]	66.47±12.66	0.84	0.430
Walking speed (m/s)	1.42±0.3[a]	0.99±0.29[b]	0.82±0.17[b]	1.09±0.37	33.46	0.000*
Step length (m)	1.26±0.18[a]	0.94±0.21[b]	0.76±0.18[c]	0.99±0.28	44.41	0.000*
Stride length (m)	2.51±0.35[a]	1.90±0.43[b]	1.57±0.44[c]	2.01±0.57	34.64	0.000*
Step duration (s)	0.92±0.23[a]	0.96±0.21[a]	0.96±0.21[a]	0.94±0.22	0.31	0.73
Stride duration(s)	1.86±0.5[a]	1.97±0.44[a]	1.85±0.39[a]	0.48±0.45	0.49	0.616
Stride frequency	0.56±0.11[a]	0.52±0.11[a]	0.56±0.11[a]	0.55±0.11	0.78	0.461
Stride velocity(m/s^2)	1.42±0.31[a]	1.03±0.29[b]	0.85±0.21[b]	1.29±0.36	27.17	0.000*
FAST						
Cadence	81.84±21.09[a]	68.65±17.69[b]	67.99±13.46[b]	72.88±18.53	6.50	0.015*
Walking speed (m/s)	1.85±0.44[a]	1.24±0.46[b]	0.93±0.22[c]	1.35±0.55	7.03	0.000*
Step length (m)	1.35±0.23[a]	1.0±0.22[b]	0.87±22[b]	1.09±0.31	30.61	0.000*
Stride length (m)	2.60±0.53[a]	2.08±0.44[b]	1.69±0.44[c]	2.13±0.60	20.96	0.000*
Step duration (s)	0.79±0.23[a]	0.94±0.24[a]	0.94±0.24[a]	0.88±0.25	3.22	0.046*
Stride duration(s)	1.57±0.47[a]	1.90±0.55[a]	1.85±0.42[a]	1.77±0.49	3.12	0.051
Stride frequency	0.68±0.19[a]	0.57±0.14[b]	0.57±0.11[b]	0.61±0.15	4.55	0.014*
Stride velocity(m/s^2)	1.77±0.48[a]	1.18±0.39[b]	0.93±0.22[b]	1.29±0.52	30.24	0.000*

DISCUSSION

The finding that HIV-seropositive individuals with mild or moderate PN had slower gait speed, shorter step length and stride length compared to those without PN, irrespective of walking pace supports the theory that afferent inputs from plantar mechanoreceptors, proprioceptors and tendon organ receptors are essential in bipedal ambulation. This is consistent with findings of (Alfuth and Rosenbaum, 2012; Kavounoudias *et al*., 1998; Aruin 2016; Quach *et al*., 2011; Takakusaki *et al*., 2017). The human gait is characterized by series of alternate and sequential steps leading to forward propulsion of the centre of gravity (Winter 1989). The ability to remain upright involves an intricate sequence of motor and sensory feedback mechanisms. Sensory detection of the body in space from visual, vestibular,

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proprioceptive and auditory cues provide feedback to allow independent mechanical adjustments in posture (Quach *et al*., 2011). As found in this study, the various deficits in gait parameters including slowed gait speed and cadence and step length have been associated with peripheral neuropathy and increased risk of falls in the elderly (Takakusaki *et al*., 2017; Callisaya 2016). According to (Quach *et al*. 2011), there is a nonlinear relationship between gait speed and falls, with a greater risk of outdoor falls in fast walkers and a greater risk of indoor falls in slow walkers. The decrease gait output found in this study could be attributed to impaired dynamic balance and fear of fall following decreased somatosensation (Manor *et al*., 2008).

The study shows that fallers possess similar gait characteristics as participants with HIV-PN, thus suggesting HIV-PN as the cause of both gait impairment and consequent falls. It is thus judged that the risk of fall in people living with HIV/AIDS increases with peripheral neuropathy, especially loss of plantar cutaneous sensation leading to elevated vibrotactile threshold. This attests to the fact that, in this study, loss of vibration perception sense otherwise known as elevated vibrotactile threshold increased the odd of fall by 10%. Patients receiving highly active antiretroviral therapy possess elevated vibrotactile threshold which proves that the incidence of distal neuropathy increases significantly with the number of drugs comprising the treatment regimen (Scarsella *et al*., 2002). Neuropathic pain has a substantial impact on physical performance and quality of life among ambulatory people living with HIV (Simmonds *et al*., 2005). This is reinforced by the findings that the odd of experiencing falls increase with report of subjective (sensory neuropathic) symptoms such as pain, aching and/or needle and pin. Result showed a linear relationship between degree of gait impairment and walking pace. While similar degree of gait impairment was observed at regular and slow walking pace, at fast walking pace, additional impairments observed include few stride frequency in those with mild HIV-PN and small cadence in those with moderate HIV-PN.

Considering that deficit in gait parameters is an independent predictor of fall, and that risk of falls increases with greater gait deficits, it might be implied, from this study, that risk of falls is greatest at fast pace. For people living with HIV-PN, walking slow is as good as walking normally as they possess similar gait output, with relatively reduced risk of fall compared to fall risk at fast walking pace. However, this finding is refuted by result obtained using the comparative field diagram, which reveals greater tendency of fall in people with mild HIV-PN compare those without HIV-PN as walking pace decrease from preferred (V2) to slow (V1). The slow speed could be seen as a strategy employ to avoid (Dingwell *et al*., 2000;Menz *et al*., 2004). Nevertheless, it may be safer for people living with HIV-PN to adapt to a slow, cautious gait characterized short step and stride length than attempt a fast pace with additional deficit in stride frequency and stride velocity. According to Erlandson *et al*.,(2012a; 2012b), PLWH exhibited impaired fast, but not preferred, gait speeds, despite being on successful HAART and those who were recurrent fallers had an even slower fast-paced gait.

The fact that fall was highest at fast walking pace also suggest that people living with HIV-PN are mainly outdoor fallers, as supported by the findings of Quach *et al.*(2011). In the work of Quach et al. (2011), gait deficits, resulting from fast walking pace, was associated with fall in outdoor or community ambulation. Depending on this, that most, if not all, falls occur during locomotion (Cavanagh et al. 1992) signifies that the people living with HIV-PN may have difficulty maintaining dynamic stability while walking. Therefore, this outcome reinforces evidence that sensory feedback plays a pivotal role in smoothing unintended irregularities that occur during unperturbed movements (Gandevia and Burke, 1994) and in adjusting step-to-step limb trajectories to maintain balance during locomotion (Ferber *et al*., 2002). However, the actual mechanism of falls in persons with HIV-PN is further elucidated by the comparative filed diagram. In this study, falls was associated with defective transition in stride velocity and frequency depicted by the reluctance region. The reluctance region is the point of reference and indicates reluctance to accelerate or decelerate, upon intention to do so, once in motion. Point at which this inertia begins defines the critical point of falls.

CONCLUSIONS

Peripheral neuropathy predisposes to gait deficits in PLWH. Degree of deficit in gait output increases

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with either fast or slow walking pace. These deficits are characterized with reluctance to accelerate or decelerate beyond usual walking pace. Moderate HIV-PN is associated with difficulty walking at fast pace while mild HIV-PN links with difficulty walk at a slow pace. The point at which this reluctance begins defines the critical point of fall. The comparative field diagram is more sensitive than one-way analysis of variance in detecting falls at slow walking pace. We recommend routine and comprehensive gait assessment, with aid of comparative filed diagram, in people with HIV-PN as this will help determine fall risk as well as inform fall preventive measures.

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AUTHOR'S CONTRIBUTIONS

Mr Martins C Nweke conceived the idea. Mr. Idika Miracle designed the proposal under the supervision of Mr Martins C. Nweke and Dr. Ezema I Charles. M.r Martins Nweke drafted the manuscript. Martins C Nweke, Mr. Chigozie Uchewoke, Mr. Aleke Marcus and Mr. Uchendu C Victor each revised the final version of the manuscript.

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