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Implementation of a Validated Peripheral Neuropathy Screening Tool in Patients Receiving Antiretroviral Therapy in Mombasa, Kenya

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Abstract. Limited objective data are available for the prevalence of peripheral neuropathy (PN) among antiretroviral (ART)–treated human immunodeficiency virus (HIV)–infected patients in resource-limited settings. A validated neuropathy-screening tool was integrated into routine ART visits at an HIV clinic in Mombasa, Kenya. Diagnosis of PN required at least one symptom and either abnormal vibratory sensation or deep tendon reflex bilaterally. Among 102 consecutively screened patients, 63% were women, 62% were receiving ART for ≤ 1 year, and 86% were receiving a stavudine (D4T)–based regimen. Thirty-seven (36%) had PN. Univariate analysis showed that current D4T use was protective against PN ($P = 0.03$) and older age was a marginal risk factor ($P = 0.05$). Multivariate analysis showed that older age was a risk factor for neuropathy ($P = 0.04$). Peripheral neuropathy was common, particularly among older HIV-infected adults in Kenya. The protective association with current D4T use likely represents survivor effect bias. Longitudinal studies using this screen will help further characterize PN in resource-limited settings.

INTRODUCTION

Patients with human immunodeficiency virus (HIV) infection are at increased risk for peripheral neuropathy (PN) for many reasons, which include use of isoniazid for tuberculosis (TB) treatment, nutritional deficiencies, use of stavudine (D4T) (and other antiretroviral agents), and HIV infection itself.[1] The debilitating impact of PN on quality of life and ability to work is considerable and sometimes permanent. In many resource-limited countries, first-line treatment for HIV infection includes D4T.[2] Recent studies from sub-Saharan Africa have found PN to be the most common side effect (range = 4.3–56%) in patients receiving D4T-based antiretroviral therapy (ART).[3–9] However, none of these studies were conducted using a validated screening tool for PN designed for use by general practitioners. We implemented a validated Brief Peripheral Neuropathy Screen (BPNS) for patients receiving ART to assess the feasibility of using this tool in routine care and to determine the prevalence of PN in our outpatient clinic population in Mombasa, Kenya.

METHODS

Study design and participants. This study was a cross-sectional study on the prevalence of PN among patients receiving ART at the Bomu Medical Center, Mombasa, Kenya. Patients were eligible for inclusion in this study if they were ≥ 15 years of age, receiving ART, and were screened during December 1, 2006–August 18, 2007. Screening was performed in either English or Kiswahili. Screening for PN was not conducted before ART was initiated in these patients. Therefore, baseline PN was not assessed.

Measures. The BPNS tool assesses subjective and objective findings consistent with PN and was developed and validated by the National Institutes of Health–funded AIDS Clinical Trials Group.[10,11] Six clinicians (two medical officers and four clinical officers) were trained on administering the questionnaire and conducting the physical examination included in the BPNS tool as a group and individually by an infectious disease specialist. Training of each clinician was conducted over one day. Only these trained clinicians screened patients for this study.

Patients were asked to rate presence and severity of symptoms, using a scale of 1 (mild) to 10 (severe) for each leg separately. Symptoms included pain, aching, or burning in feet and/or legs; "pins and needles" in feet and/or legs; and numbness in feet and/or legs. The single highest of the six scores (three for each leg) was then converted to a subjective peripheral neuropathy grade as follows: symptoms absent = grade 0, score of 1–3 = grade 1, score of 4–6 = grade 2, and score of 7–10 = grade 3. Symptoms did not have to be bilateral to be graded as ≥ 1.

Objective findings included in the BPNS were loss of vibration perception and abnormal ankle deep tendon reflexes. Vibration perception was evaluated using a 128-Hz tuning fork, maximally struck and applied at the great toe distal interphalangeal joint of each foot. Vibration sense was defined as normal for a vibration felt for > 10 seconds, mild loss for a vibration felt for 6–10 seconds, moderate loss for a vibration felt for ≥ 5 seconds, and severe loss for no feeling of vibration. Ankle reflexes were defined as absent, hypoactive, normal, hyperactive, or clonus.

The primary outcome of interest, the presence of PN, was defined as the combination of a subjective neuropathy grade greater than 0 and at least one bilateral objective finding.[10] Secondary outcomes included each of the components of the overall assessment: 1) presence of symptoms, 2) abnormal vibratory sense, and 3) abnormal deep tendon ankle reflex. Using univariate and multivariate methods we assessed the influence of the following factors on the presence of primary and secondary outcomes: age, sex, baseline weight, height and body mass index at time of ART initiation, baseline CD4 cell count at time of ART initiation, current or past use of D4T treatment, and time receiving ART. Clinical diagnosis of AIDS was defined as having a CD4 cell count < 200 or clinical stage IV by World Health Organization criteria.[12] Those variables with $P \leq 0.20$ in univariate analyses were included in the multivariate analysis. All statistical analysis was performed using STATA version 9.0 software (STATA Corp., College Station, TX).

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The study was reviewed and approved by the Institutional Review Board for New York University School of Medicine and the Ethics Review Committee of the Kenyatta National Hospital Nairobi, Kenya.

RESULTS

The addition of the PN screening added approximately five minutes to the clinic visit. One hundred five persons were screened in the study interval and 102 were included in the analysis. Two patients were excluded because accurate vibration scores were not recorded and one patient was excluded because a deep tendon reflex score was not recorded. Baseline characteristics of the study population are shown in Table 1. Sixty-four (63%) of the 102 patients were female; the median age was 39 years (interquartile range [IQR] = 33–46 years). Median baseline CD4 cell count was 143 cells/mm^3 (IQR = 76–199 cells/mm^3), and thirty-five (34%) of patients had a baseline CD4 cell count less than 100 cells/mm^3. The median time since initiation of ART was 10.2 months (IQR = 5–16.4 months). Eighty-eight (86%) patients were receiving a D4T (40 mg)–based ART regimen at the time of screening, 12 (12%) were receiving zidovudine-based ART, and two (2%) were receiving tenofovir-based ART. Eight (57%) of the 14 patients not receiving D4T at the time of screening had received D4T in the past. Of these eight patients, six (75%) had had D4T discontinued because of neuropathy and two (25%) because of concomitant TB therapy. Of the six patients with no prior or current D4T use, three were transferred into our clinic on a non-D4T based regimen, one was pregnant, one had diabetes, and one was on concomitant TB therapy with baseline neuropathy. Seventeen (16.7%) patients had received isoniazid in the past and one (1%) patient was receiving isoniazid at the time of the PN screening.

Sixty-nine (68%) of 102 patients reported subjective neuropathic symptoms. Twenty-six (38%) of 69 patients reported grade 1 severity, 29 (42%) reported grade 2 severity, and 14 (20%) reported grade 3 severity. Fifty-eight (84%) of 69 patients with subjective symptoms were receiving D4T-based therapy compared with 30 (91%) of the 33 patients without subjective symptoms (P = 0.35). Patients who reported subjective symptoms were slightly older than those who did not (P = 0.12), and the median time receiving ART among patients with subjective symptoms was 10.3 months compared with 9.8 months among those without symptoms (P = 0.72).

Forty-two (41%) of 102 patients had bilateral loss of vibratory sensation on examination and 46 (45%) had unilateral loss. Twenty-nine (69%) of 42 patients with bilateral abnormal vibratory sensation showed mild loss, 9 (21%) showed moderate loss, and 4 (10%) showed severe loss. Thirty-one (74%) of 42 patients with abnormal vibratory sensation were receiving D4T-based therapy at the time of screening compared with 57 (95%) of the 60 patients with normal vibratory sensation (P = 0.006). Seven (88%) of the eight patients who had received D4T in the past but subsequently changed to an alternative regimen had abnormal vibratory sensation at the time of this screening. The median time receiving ART among patients with abnormal vibratory sensation was 10 months compared with 10.3 months among those with normal vibratory sensation (P = 0.84). Twenty-five (25%) of 102 patients had either absent or hypoactive ankle reflexes bilaterally, and 27 (26%) had absent or hypoactive ankle reflexes unilaterally. Eighteen (72%) of the 25 patients with reduced ankle reflexes bilaterally were receiving D4T-based therapy compared with 70 (91%) of the 77 patients without abnormal ankle reflexes (P = 0.02). The median time receiving ART among patients with abnormal ankle reflexes was 11 months compared with 10.2 months among those with normal reflexes (P = 0.43). No patient had reports of hyperactive reflexes or clonus.

Thirty-seven (36%) of 102 patients had PN (presence of subjective symptoms and at least one objective finding bilaterally). Twenty-two (59%) were female. Median baseline weight was 56 kg (IQR = 50–63 kg), and median baseline CD4 cell count at time of ART initiation was 138 cells/mm^3 (IQR = 58–201 cells/mm^3). Seven (19%) had received INH in the past or at the time of the screening. Thirty-three (89%) had a history of D4T use. Twenty-eight (76%) patients with PN were receiving D4T at the time of screening compared with 60 (92%) of patients without PN (P = 0.03). Five (14%) patients had received D4T in the past compared with three (5%) of patients without PN (P = 0.12). The reasons for switch from D4T for these patients included neuropathy (n = 4) and concomitant TB therapy (n = 1). Median time since initiation of ART in patients with PN was 9.3 months (IQR = 4.9–15.8 months) compared with 10.5 months (IQR = 5.1–18.2 months) in patients without PN (P = 0.45).

Eleven (33%) of the 33 patients who denied having symptoms of neuropathy had abnormal findings on physical examination: four had abnormal bilateral ankle reflexes, three had abnormal bilateral vibratory sensation, and four had both findings. In contrast, 32 (46%) of 69 patients who reported symptoms of neuropathy had normal findings on physical examination. We determined the relationship between the severity of subjective symptoms and presence of abnormal objective findings. There was a positive association between grade of subjective symptoms and the finding of abnormal vibratory sense on examination (grade 0 = referent group; grade 1 odds ratio [OR] = 0.9, 95% confidence interval [CI] = 0.2–3.2); grade 2 OR = 5.3, 95% CI = 1.8–16.9; and grade 3 OR = 48.3, 95% CI = 7.7–958.1). There was no significant association between subjective grade and the presence of abnormal ankle

TABLE 1

Baseline characteristics of 102 patients receiving antiretroviral therapy screened for peripheral neuropathy, Mombasa, Kenya*

Characteristic	Value
Median (quartile) years of age	39 (33–46)
Female	64 (63%)
Median (quartile) baseline CD4 cell count/μL	143 (76–199)
Median (quartile) baseline weight, kg	57 (51–63)
Median (quartile) baseline height, cm	164.5 (156.8–170)
Median (quartile) body mass index, kg/m^2	20.9 (19.1–23.6)
Current NRTI backbone	
D4T	88 (86%)
AZT	12 (12%)
TDF	2 (2%)
Median (quartile) time since initiation of ART, months	10.2 (5–16.4)
Clinical diagnosis of AIDS	63 (62%)
History of treatment with isoniazid (INH)	
Prior INH therapy	17 (17%)
Current INH therapy	1 (1%)
No history of INH therapy	84 (82%)
History of diabetes	0 (%)

*Values are no. (%) unless otherwise indicated. ART = antiretroviral therapy; NRTI = nucleoside reverse transcriptase inhibitor; D4T = stavudine; AZT = zidovudine; TDF = tenovir; INH = isoniazid.

TABLE 2
Factors associated with neuropathy in patients receiving antiretroviral therapy, Mombasa, Kenya*

Predictor variable	Neuropathy: Present, n = 37 (36%)	Neuropathy: Absent, n = 65 (64%)	Univariate analysis: Odds ratio (95% confidence interval)	*P*
Median (quartile) years of age	42 (35–49)	38 (33–44)	1.0 (1.0–1.1)	0.05
Median (quartile) months receiving ART	9.3 (4.9–15.8)	10.5 (5.1–18.2)	1.0 (0.9–1.0)	0.45
Female	22 (59%)	42 (65%)	1.2 (0.5–2.9)	0.61
Median (quartile) baseline kilograms of weight	56 (50–63)	57 (51–63)	1.0 (0.96–1.03)	0.79
Median (quartile) baseline centimeters of height	165 (159.5–170)	161.5 (155.5–170)	1.0 (0.98–1.06)	0.38
Median (quartile) baseline CD4 cell count	138 (58–201)	144 (95–199)	1.0 (0.99–1.0)	0.32
CD4 cell count < 100 cells/mm^3	16 (43%)	19 (29%)	1.8 (0.8–4.3)	0.15
Clinical diagnosis of AIDS	22 (59%)	41 (63%)	0.9 (0.4–2.0)	0.72
Any D4T use	33 (89%)	63 (97%)	0.3 (0.05–1.5)	0.13
Current D4T use	28 (76%)	60 (92%)	0.3 (0.08–0.8)	0.03
Past D4T use	5 (14%)	3 (5%)	3.2 (0.7–14.4)	0.12
Current or past INH use	7 (19%)	11 (17%)	1.1 (0.4–3.3)	0.80

*Values are no. (%) unless otherwise indicated. ART = antiretroviral therapy; AIDS = acquired immunodeficiency syndrome; D4T = stavudine; INH = isoniazid. Neuropathy is defined as presence of subjective symptoms and at least one objective finding of neuropathy from the Brief Peripheral Neuropathy Screen.

reflexes (grade 0 = referent group; grade 1 OR = 0.6, 95% CI = 0.1–2.1; grade 2 OR = 1.2, 95% CI = 0.4–3.8; and grade 3 OR = 1.7, 95% CI = 0.4–6.7).

Univariate analyses for primary and secondary outcomes are shown in Tables 2–5. In univariate analysis, older age was a marginally significant risk factor for PN ($P = 0.05$), and current D4T use was significantly protective against PN ($P = 0.03$). In multivariate analysis, older age was the only significant risk factor for neuropathy ($P = 0.04$) when controlling for variables found to have a $P < 0.2$ in univariate analysis (age, baseline CD4 cell count < 100 cells/mm^3, and D4T use). In univariate analysis of our secondary outcomes, current D4T use and past D4T use were associated with abnormal vibratory sense (Table 4) and age, and current or past D4T use were associated with abnormal ankle reflexes (Table 5). Multivariate analyses showed an association with current use of D4T and having normal vibratory sensation ($P < 0.01$) and normal ankle reflexes ($P = 0.02$), controlling for variables found in univariate analysis to have a $P < 0.2$ (Tables 4 and 5).

Eleven (10.7%) of patients had a change in their ART regimen because of a positive result on PN screening. All were on a D4T-based regimen at the time of screening and the regimen was changed to zidovudine (eight patients) or tenovir (three patients).

We elicited opinions about the BPNS among the trained providers through a basic questionnaire (Table 6). All found the screening tool to be either extremely or somewhat useful in clinical practice; all found the ankle reflexes to be the most difficult component of the screen (and during the training similar difficulties required additional time practicing on colleagues prior to the start of screening); and most found it to be only mildly or not at all inconvenient to incorporate into a clinic visit.

DISCUSSION

The BPNS has been validated in HIV-infected patients using physiologic (quantitative sensory threshold testing) and pathologic (epidermal nerve fiber density) testing as the gold standards.[10] That study found that patients with symptoms of PN but without abnormal vibration sensation or deep tendon reflex did not differ significantly from asymptomatic patients in their measurements in quantitative sensory threshold testing and epidermal nerve fiber density testing. In contrast, patients with symptoms and bilateral abnormal ankle reflexes or vibration sensation were most likely to also have abnormal physiologic and pathologic testing. Using this screening and the definition of PN used in the validation study,[10] we observed

TABLE 3
Factors associated with subjective symptoms in patients receiving antiretroviral therapy, Mombasa, Kenya*

Predictor variable	Subjective symptoms: Present, n = 69 (68%)	Subjective symptoms: Absent, n = 33 (32%)	Univariate analysis: Odds ratio (95% confidence interval)	*P*
Median (quartile) years of age	41 (34–48)	38 (32–44)	1.0 (1.0–1.1)	0.12
Median (quartile) months receiving ART	10.3 (5.1–16.4)	9.8 (4.4–15.4)	1.0 (1.0–1.1)	0.72
Female	45 (65%)	19 (58%)	0.7 (0.3–1.7)	0.46
Median (quartile) baseline kilograms of weight	56 (50–63)	58 (52–62)	1.0 (0.9–1.0)	0.57
Median (quartile) baseline centimeters of height	161.5 (155–169)	168.5 (160.5–172)	1.0 (0.92–1.01)	0.12
Median (quartile) baseline CD4 cell count	144 (58–199)	140 (99–179)	1.0 (0.99–1.0)	0.41
CD4 cell count < 100 cells/mm^3	26 (38%)	9 (27%)	1.6 (0.7–4.0)	0.30
Clinical diagnosis of AIDS	44 (64%)	19 (58%)	1.3 (0.6–3.0)	0.55
Any D4T use	64 (93%)	32 (97%)	0.4 (0.04–3.6)	0.41
Current D4T use	58 (84%)	30 (91%)	0.5 (0.1–2.0)	0.35
Past D4T use	6 (9%)	2 (6%)	1.5 (0.3–7.7)	0.65
Current or past INH use	12 (17%)	6 (18%)	0.9 (0.3–2.8)	0.92

*Values are no. (%) unless otherwise indicated. ART = antiretroviral therapy; AIDS = acquired immunodeficiency syndrome; D4T = stavudine; INH = iosniazid.

TABLE 4
Factors associated with abnormal vibratory sense in patients receiving antiretroviral therapy, Mombasa, Kenya*

Predictor variable	Vibratory sensation		Univariate analysis	
	Abnormal, n = 42 (41%)	Normal, n = 60 (59%)	Odds ratio (95% confidence interval)	*P*
Median (quartile) years of age	42 (34–49)	38 (33–44)	1.0 (1.0–1.1)	0.08
Median (quartile) months receiving ART	10 (5.1–15.8)	10.3 (4.7, 17.6)	1.0 (0.9–1.0)	0.84
Female	27 (64%)	37 (62%)	0.9 (0.4–2.0)	0.79
Median (quartile) baseline kilograms of weight	57 (50–63)	57 (51, 64)	1.0 (1.0–1.0)	0.86
Median (quartiles) baseline centimeters of height	165.3 (159.5–170)	161 (155.3, 171.5)	1.0 (0.98–1.07)	0.26
Median (quartile) baseline CD4 cell count	144 (75–201)	141 (80, 199)	1.0 (0.99–1.0)	0.89
CD4 cell count < 100 cells/mm^3	15 (36%)	20 (33%)	1.1 (0.5–2.5)	0.80
Clinical diagnosis of AIDS	24 (57%)	39 (65%)	0.7 (0.3–1.6)	0.42
Any D4T use	38 (91%)	58 (97%)	0.3 (0.06–1.9)	0.21
Current D4T use	31 (74%)	57 (95%)	0.1 (0.04–0.6)	< 0.01
Past D4T use	7 (17%)	1 (2%)	11.8 (1.4–100)	0.02
Current or past INH use	9 (21%)	9 (15%)	1.5 (0.6–4.3)	0.40

*Values are no. (%) unless otherwise indicated. ART = antiretroviral therapy; AIDS = acquired immunodeficiency syndrome; D4T = stavudine; INH = isoniazid.

that 36% of patients in Kenya receiving ART had subjective and objective findings of PN; 46% of patients who reported symptoms of neuropathy had no evidence of PN on physical examination; and 33% of patients without symptoms had evidence of PN on physical examination. The latter group may represent patients with early PN, although only prospective examinations using the BPNS could confirm this definitively.

In resource-rich countries, PN complicates therapy in approximately 10–30% of patients receiving D4T or didanosine.[1] However, World Health Organization guidelines and many national guidelines in resource-limited countries recommend D4T or zidovudine as first-line treatment with recent recommendations to reduce the dose of D4T to 30 mg to minimize adverse events.[2] Several studies from sub-Saharan Africa have also found PN to be a significant side effect in patients receiving D4T-based ART (range = 4.3–56%)[3–8,13] and the most common reason for switching regimens because of adverse events.[5] However, use of a validated screen for neuropathy was not reported in most of these studies. A recent study conducted in South Africa found a 30% prevalence of symptomatic PN among HIV-infected adults, although they added the assessment of pinprick, muscle stretch reflexes, and strength to the BPNS tool and required the presence of symptoms for at least two weeks. This supplementation to the BPNS tool decreases the practicality of using the screening tool in busy clinics in resource-limited settings outside of a study setting. In Malawi, 56% of 264 patients receiving D4T, lamivudine, and nevirapine for at least six months reported symptoms of numbness or pain in the lower extremities;[8] however, objective findings were not reported. In Uganda, investigators reported that 36% of 894 patients receiving D4T-based ART had PN; however, a validated screen was not used.[4]

We found older age to be significantly associated with the presence of neuropathy as measured by the BPNS, even when adjusted for any history of D4T use. This association has been observed in cohort studies in resource-limited and resource-rich settings.[4,13–15] The use of a validated screen in our study provides strength to this association previously found in the few studies conducted in patients in Africa.[4,14,15] We also found that current D4T use was protective against signs of neuropathy (vibratory sense and ankle reflexes). Although this finding seems counterintuitive, this likely represents survivor bias, whereby patients receiving D4T in whom neuropathy did not develop continued receiving D4T-based regimens at the time of the study screen, and those receiving D4T in whom neuropathy developed before study entry were switched to a non-D4T-based regimen before screening. Longitudinal data, obtained by applying this validated screening tool from time of ART initiation every 3–6 months, may provide more accurate assessment of the incidence of and the rapidity with which PN develops in patients living in resource-limited settings. Furthermore, a baseline PN screen before ART is initiated would also help delineate between ART and non-ART associated PN in this population.

TABLE 5
Factors associated with abnormal ankle deep tendon reflex in patients receiving antiretroviral therapy, Mombasa, Kenya*

Predictor variable	Ankle deep tendon reflex		Univariate analysis	
	Abnormal, n = 25 (25%)	Normal, n = 77 (75%)	Odds ratio (95% confidence interval)	*P*
Median (quartile) years of age	44 (36–50)	39 (33–44)	1.1 (1.0–1.1)	0.04
Median (quartile) months receiving ART	11.0 (7.8–18.2)	10.2 (4.4–15.4)	1.0 (1.0–1.1)	0.43
Female	14 (56%)	50 (65%)	1.5 (0.6–3.6)	0.42
Median (quartile) baseline kilograms of weight	61 (52–64)	57 (51–62)	1.0 (1.0–1.1)	0.12
Median (quartile) baseline centimeters of height	168.5 (161.5–172)	161.5 (155–170)	1.1 (1.0–1.1)	0.06
Median (quartile) baseline CD4 cell count	133 (36–188)	146 (88–201)	1.0 (0.99–1.0)	0.11
CD4 cell count < 100 cells/mm^3	12 (48%)	23 (30%)	2.2 (0.9–5.5)	0.10
Clinical diagnosis of AIDS	16 (64%)	47 (61%)	1.1 (0.4–2.9)	0.79
Any D4T use	23 (92%)	73 (95%)	0.6 (0.1–3.7)	0.61
Current D4T use	18 (72%)	70 (91%)	0.3 (0.08–0.8)	0.02
Past D4T use	5 (20%)	3 (4%)	6.2 (1.4–28.0)	0.02
Current or past INH use	4 (16%)	14 (18%)	0.9 (0.3–2.9)	0.80

*Values are no. (%) unless otherwise indicated. ART = antiretroviral therapy; AIDS = acquired immunodeficiency syndrome; D4T = stavudine; INH = isoniazid.

TABLE 6
Provider feedback on feasibility of peripheral neuropathy screening, Mombasa, Kenya

Question	Responses (n = 4)
Was the screen inconvenient to use during a clinic visit?	
Extremely inconvenient	0
Somewhat inconvenient	1
Mildly inconvenient	1
Not at all inconvenient	2
Mean time to administer the screen, minutes (range)	4 (2–6)
What was the most difficult component of the screen?	
Ankle reflexes	4
Tuning fork rest	0
Symptom screening	0
Do you find the PN screen to be useful in clinical practice*?	
Extremely useful	3
Somewhat useful	1
Mildly useful	0
Not at all useful	0

* PN = peripheral neuropathy.

Our results may be generalizable to other HIV treatment sites in sub-Saharan Africa for several reasons. Consecutive patients were enrolled into the study and none refused. However, we did not randomly assign patients to undergo screening. Therefore, selection bias is unlikely to be a major factor but is not negligible. Our study was performed at a single clinic site. However, results may be generalizable because the demographic (e.g., age, sex) and clinical (e.g., baseline CD4 cell count < 200 cells/mm^3, antiretroviral choices) profiles of our patients are similar to those in other populations in Africa.[16]

Several limitations of this study should be considered. First, the cross-sectional design limits our ability to assess the temporal relationship between risk factors and the presence of PN and baseline screening for PN prior to initiation of ART was not available. Furthermore, because patients were not receiving D4T at the same time, a survivor effect bias may have led to an underestimation of the risk of D4T use for developing PN.[17] In other words, those in whom adverse events from D4T use developed prior to the study may have been switched to a non-D4T-based regimen before the study examination, and those who tolerated D4T well remained on that regimen. Second, our small sample size likely prevented identification of risk factors for PN, although previous studies have reported a significantly higher rate of PN among patients with lower CD4 cell count, of older age, and among those receiving treatment for TB.[18] Finally, reporting bias in patient report of subjective neuropathic symptoms may lead to under reporting or over reporting.

In summary, a validated and concise screening tool comprised of subjective and objective measures of PN can be easily integrated into routine care by general practitioners in an outpatient HIV clinic with limited resources. Clinicians were easily briefed on the use of the screening tool and were able to incorporate screening within the time constraints of follow-up visits in a busy urban clinic in Kenya. Annual or semi-annual screening for PN among patients with HIV infection may enable earlier detection of PN and timely changes in management to maintain quality of life by preventing progression to debilitating symptoms, particularly in older patients. Finally, the BPNS can be an important tool for further study on the rapidity of onset of PN among HIV-infected patients in Africa.

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