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The Spectrum of Neurological Disorders in a Zambian Tertiary Care Hospital

Omar K. Siddiqi, MD, Masharip Atadzhanov, MD, PhD, FRCP, Gretchen L. Birbeck, MD, MPH, DTMH, FAAN, and Igor J. Koralnik, MD

From the Department of Neurology (O.K.S., I.J.K.), Beth Israel Deaconess Medical Center, Boston, MA; University of Zambia (M.A.), Lusaka, Zambia; Michigan State University (G.L.B.), East Lansing, MI

Abstract

Objectives—To define the spectrum of inpatient and outpatient neurological illness in a Zambian tertiary care facility where HIV is endemic.

Methods—A retrospective period prevalence study of patients seen by the consulting neurologist between 1/2/06 – 12/20/06 at the University of Zambia's University Teaching Hospital (UTH).

Results—443 inpatients and 368 outpatients were seen during this period. Overall, 160 (19.7%) patients underwent HIV testing: 125 (15.4%) HIV⁺ and 35 (4.3%) HIV[−]. The other 651 (80.3%) patients were untested. The most common inpatient neurological diseases among HIV⁺ patients were infectious diseases 26 (38.8%), neuropathy/radiculopathy 10 (10.4%), cerebrovascular disease 6 (9.0%), and myelopathy 5 (7.5%). The most common inpatient neurological diseases in the general population were cerebrovascular disease 62 (16.5%), infectious diseases 47 (12.5%), neuropathy/radiculopathy 37 (9.8%), and seizures/epilepsy 27 (7.2%). In the outpatient population, the most common neurological illnesses in HIV⁺ patients were neuropathy/radiculopathy 18 (31.0%), cerebrovascular disease 8 (13.8%), dementia/neurodegenerative 8 (13.8%), and encephalopathy 7 (12.1%). Outpatients in the general population most commonly had headaches/cephalgias 60 (19.4%), movement disorders 47 (15.2%), neuropathy/radiculopathy 43 (13.8%), and seizures/epilepsy 39 (12.6%).

Conclusions—HIV-infected individuals are a sizeable group among neurology patients in Zambia, and they are affected by a different disease spectrum than the general population. Infectious diseases make up the largest percentage of inpatient neurological illness. Non-infectious causes are responsible for the majority of outpatient neurological cases. Emphasis should be placed on treatment of both infectious and non-infectious neurological illnesses. The most common outpatient neurological conditions are symptomatically treatable with routinely available medications.

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Corresponding author: Dr. Omar Siddiqi, Beth Israel Deaconess Medical Center, W/BA-5, 330 Brookline Avenue, Boston, MA 02215. Phone# (617) 667-2395. Fax# (617) 632-8931. osiddiqi@bidmc.harvard.edu.

Co-author: ikoralni@bidmc.harvard.edu (I.J.K.), masharip@yahoo.com (M.A.), Gretchen.Birbeck@hc.msu.edu (G.L.B.).

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Keywords

epidemiology; prevalence; infections; HIV; Zambia; Africa

Introduction

Developing countries carry a dual burden of neurological illness. Conditions are both under-recognized and under-treated. Epidemiologic data from the Global Burden of Disease illustrates that there is a significant amount of infectious and non-infectious neurological illness in the developing world. Population-based epidemiological surveys are difficult to perform in Africa due to logistical and resource limitations. There are a handful of hospital-based studies from the pre and post-HIV era that attempt to quantify the burden of neurological disease in sub-Saharan Africa.^{1,2,3,4,5,6} These are summarized in Table 1. This information is valuable because it provides focus on potential areas of intervention as well as identifying regional variations among developing countries in the epidemiological transition from infectious to non-infectious diseases.

A major problem in developing countries is the lack of neurological expertise. In African nations the average ratio of neurologists to the general population is on the order of 1:3.4 million with 11 nations reporting no neurologist at all. By comparison, the ratio of neurologists to the general population in the US is 1:26,200.⁷ This highlights both the need for neurological care and the barriers towards defining neurological illness.

At present, the largest area of focus for U.S. governmental funding of public health interventions in Sub-Saharan Africa is HIV, tuberculosis, and malaria.⁸ All of these diseases can be associated with some degree of neurological morbidity/mortality. Additionally, non-infectious neurological illness is increasingly common and may provide unique epidemiologic insights on disease. One way to begin to understand the true nature of disease is to evaluate its prevalence in the inpatient and outpatient settings.

Zambia lies in Southern Africa and is bordered by 8 other African nations. The population is made up of more than 11 million people. There is one full-time practicing adult neurologist in the entire country based at the main teaching hospital. We conducted a study to assess the spectrum of inpatient and outpatient neurological illness in a Zambian tertiary care facility. Once the scale of neurological disease is established in this setting, advocacy efforts can be made to obtain appropriate resources targeted towards preventive and therapeutic interventions.

Methods

We reviewed the records of all adult outpatients in the neurology clinic as well as all adult inpatient neurology consultations seen at the University Teaching Hospital (UTH) in Lusaka, Zambia from 1/2/06 – 12/20/06. UTH is the major teaching hospital for the University of Zambia, School of Medicine and the main tertiary care center in Zambia. It has outpatient specialty and subspecialty clinics. There is also a large inpatient service that is divided into medical, surgical, and OB/GYN wards. Adult patients are initially admitted to these services and if there is a neurological issue requiring further clarification or management, senior ward physicians call the consulting neurologist. The consulting neurologist keeps a log of all inpatients and outpatients seen with diagnoses recorded at the time of consultation. Available laboratory studies included complete blood count, serum electrolytes, kidney and liver function tests, coagulation studies, gram stain, acid-fast stain, bacterial/fungal/mycobacterium culture, and sensitivity. Active HIV infection in Zambia is diagnosed by the Abbot Determine rapid

HIV test followed by a confirmatory Uni-Gold rapid HIV test. CSF studies include gram stain, cultures, India ink stain, cell count/differential, total protein, glucose, and cryptococcal antigen. PCR for detection of viral DNA is not available. Radiological testing includes CT, CT myelography, and plain films. Some patients obtain MRI studies in neighboring countries.

We placed all patients seen by the neurologist into general diagnostic categories based on their primary presentation, physical exam, and subsequent studies. Certain cases had a distinct clinical diagnosis that laboratory and radiological data supported. A number of cases did not have a final clinical diagnosis due to resource limitations. Based on the neurological evaluation, we could still place some of these cases into a broad diagnostic category. Electrophysiological studies were not available. When it was unclear what a patient had or he/she could not be placed into a diagnostic category with great certainty than we recorded this as “diagnosis unclear”. If patients had a condition that represented < 1% of the study population, we grouped them into a category labeled as “other conditions”. Below is a detailed description of the more common disease categories seen in both inpatients and outpatients:

The “infectious” category represented patients whose primary presentation was related to an underlying infection of the nervous system such as cryptococcal meningitis, toxoplasmic encephalitis, or cerebral malaria. “Neuropathy/radiculopathy” represented a heterogeneous group of peripheral nervous system disorders including diabetic neuropathy, AIDP/CIDP, plexopathies, and radiculopathies. “Cerebrovascular” disease included ischemic stroke, hemorrhagic stroke, and transient ischemic attacks. “Demyelination” was restricted to the central nervous system and included cerebral demyelination, acute disseminated encephalomyelitis, and transverse myelitis. “Myelopathy” was a broad category that included patients with obvious signs of spinal cord dysfunction such as leg weakness, bowel/bladder symptoms, or sensory level without any further details to clarify the diagnosis. “Dementia/Neurodegenerative” included AIDS-Dementia Complex, Alzheimer’s disease, Huntington’s disease, and cerebellar degeneration. “Encephalopathy” was defined as cognitive dysfunction of unknown origin whose time course fit an acute/subacute confusional state.

We compared the HIV⁺ population to the general population for both inpatients and outpatients to see variations in diagnostic categories. We defined the general population as patients that were known to be HIV⁻ along with patients whose HIV status was unknown. These patients were grouped together due to the relatively small number of patients that were known to be HIV⁻. Statistical analysis was performed using a Fischer’s exact test – two tailed (<http://www.langsrud.com/fisher.htm>) comparing the prevalence of diseases between the HIV⁺ patients and the general population. A P value less than 0.05 was considered statistically significant.

Results

The neurologist saw a total of 443 inpatients and 368 outpatients during the study period. The relevant demographic data of the study population are presented in Table 2. The median age of patients in both inpatient and outpatient population was 39. A total of 125 (15.4%) patients were HIV⁺: 67 (15.1%) inpatients and 58 (15.8%) outpatients. Of the 686 patients in the general population, 35 (5.1%) patients underwent HIV testing and were confirmed as HIV⁻ with the remaining 651 (94.9%) untested. Men and women were equally represented. Although there was a trend for a higher number of women in the outpatient population, the percentage of men who were HIV⁺ was higher. In post-hoc analysis, this reached statistical significance ($p < 0.003$).

Table 3 lists the inpatient diagnostic categories among HIV⁺ patients and the general population. As expected, infectious diseases accounted for the largest percentage 38.8% ($n=26$) of inpatient neurological diagnoses in HIV⁺ population, compared to 12.5% ($n=47$) in the

general group ($p < 0.001$). Among infections seen in HIV⁺ patients, the most common were cryptococcal meningitis ($n=12$), toxoplasmic encephalitis ($n=3$), and tuberculosis ($n=3$). The most common infections seen in the general population were tuberculosis ($n=16$), neurocystercosis ($n=4$), syphilis ($n=3$), and bacterial meningitis ($n=3$).

There was a trend for an increased number of myelopathy cases in the HIV⁺ group 5 (7.5%) vs. the general population 10 (2.7%) ($p=0.06$).

Table 4 lists the outpatient diagnostic categories among HIV⁺ patients and the general population. The most frequent diagnostic category in HIV⁺ individuals was neuropathy/radiculopathy 18 (31.0%) which was significantly higher than in the general population 43 (13.8%) ($p=0.003$). Similar to inpatients, the 4 (6.9%) cases of myelopathy were significantly higher in the HIV⁺ patients compared to the one (0.3%) case in the general population ($p=0.002$).

As expected dementia was more frequent in HIV⁺ patients 8 (13.8%) compared to the general population 9 (2.9%) ($p=0.002$), and most cases were felt to be HIV-related. This was the case as well for patients affected with encephalopathy (12.1% vs. 1.3%, $p=0.04$). Surprisingly, HIV⁺ patients had a higher prevalence of cerebrovascular disease compared to the general patients (13.8% vs. 5.8%, $p=0.04$). There was no significant difference in the age of the patients in these two groups. In most cases, the precise etiology of the ischemic event could not be determined.

Finally, headaches, movement disorders, and seizures were significantly more frequent in the general population than in HIV⁺ patients.

Neoplasms/Neoplastic disease did not significantly differ between HIV⁺ patients or the general population. However, the average age of patients with neoplasms/neoplastic disease in the entire study was surprisingly young at 43 and did not differ between HIV⁺ patients and general patients.

We placed 17 inpatients and 21 outpatients into the category of “other conditions”. None of these patients were HIV⁺.

Discussion

This study illustrates that outpatient and inpatient neurological diseases in an urban setting of Sub-Saharan Africa are distinctly different between HIV⁺ patients and the general population. The median age of patients was similar in both groups but considerably younger than neurology patients usually seen in developed countries. Indeed, the life expectancy of a Zambian citizen is 43.0, compared to 77.8 in the United States.^{9,10}

As expected, infectious diseases or their associated complications account for the largest percentage 16.5% ($n=73$) of inpatient neurological illness among all individuals. This percentage is similar to that seen in published data from an academic tertiary care facility in Addis Ababa, Ethiopia.⁵

Non-infectious neurological illness represented a substantial number of the inpatients. Cerebrovascular disease was the most common neurological diagnosis in the general population. The etiology is certainly different to that seen in the U.S. given the demographic of patients. The average age for an inpatient stroke was 50, and it was not significantly different among HIV⁺ individuals and those in the general population. This finding was somewhat surprising as ischemic stroke in HIV⁺ patients has been previously reported as occurring at a much younger age in a comparable health center in Blantyre, Malawi.¹¹ However, our study

population had a number of patients with cerebrovascular disease who were likely HIV⁺ but never had formal testing.

The global burden of epilepsy is well described and our data shows that seizures represent both an inpatient and outpatient problem. Of all neurology patients, 69 (8.5%) suffered from seizures. Our data did not distinguish between epilepsy, idiopathic, acute symptomatic, or remote symptomatic seizures. The prevalence of seizures in our study is similar to data published from other hospital based studies on urban adult populations in Dar es Salaam, Tanzania² and Addis Ababa, Ethiopia.⁵ The prevalence rate is also lower in comparison to other hospital based studies from sub-Saharan Africa that combine data from both adult and pediatric populations.^{4,6}

It was not surprising that HIV⁺ inpatients suffered disproportionately from infectious diseases given their greater susceptibility to opportunistic infections. The greater percentage of myelopathy cases among HIV⁺ inpatients and outpatients could be explained by the presence of HIV-1 associated vacuolar myelopathy. However, this is only speculative as there is no histological or imaging data to support this.

The outpatient neurological illness was different in terms of the predominance of non-infectious causes. The most common outpatient diagnoses in the general population are similar to those neurological problems that might be seen in a resource rich setting. Greater than 50% (n=189) of the conditions were accounted for by headache, neuropathy/radiculopathy, movement disorders, and seizures. After these four conditions, the next most frequently seen patients were those with cerebrovascular disease at 5.8% (n=18).

As expected, HIV⁺ outpatients suffered more from neuropathy/radiculopathy, dementia, and encephalopathy compared to the general population. Neuropathy and cognitive changes are well established complications of HIV infection. While patients with encephalopathy had more subacute/acute cognitive changes compared to the progressive cognitive decline in the dementia category, these two groups likely represent a continuum.

HIV⁺ patients with dementia were younger than their counterparts in the general population, with an average age of 50 vs. 68, respectively. Cognitive impairments have previously been reported as common among persons living with AIDS in Zambia.¹²

The rationale behind placing the patients into broad diagnostic categories was that this would give the clearest perspective on the type of patients that are seen. The assumption is that a trained neurologist can place most patients into a diagnostic category, with the aid of the history, a neurological exam, and limited testing. A total of 25 patients in both groups were placed in the category of diagnosis unclear. Prior hospital based studies of neurological disorders from Ethiopia and Tanzania have also grouped patients in diagnostic categories with separate categories for cases of diagnostic uncertainty.^{5,6}

Outpatient data may be better categorized as these patients were followed and their presentations may have become clearer on subsequent visits. Given the predominant non-infectious nature of the outpatient diagnoses, different resources should be allocated to this patient population. Headache, neuropathy, and seizures all have relatively inexpensive symptomatic treatments that can be used in this setting. Moreover, non-neurologists could at least be trained to take care of these conditions.

There are numerous areas that can be targeted for both short term and long term improvement. Proven therapies that are available need to be maximized. Common inpatient conditions such as cerebrovascular disease, seizure, and meningitis may benefit from protocols that make it easier for a non-neurologist to treat. Outpatient providers could be trained on the most common

conditions that appear in that setting. There would be an enormous benefit from collaborations between academic centers in the developed countries with those in developing countries in terms of intellectual exchange, resident education, and research.

In terms of treatment, many medications considered to be standard of care in developed countries are not available on the hospital formulary. Medications are provided free by the government; as a result the availability is limited by cost. For example, late stage Parkinson's patients are treated with bromocriptine because levodopa/carbidopa is too costly to obtain. A very small fraction of patients can get more complete neurological care if they have the finances to travel to a nearby country with greater resources such as South Africa.

There are multiple limitations to this study. It was completed at only one institution that is a tertiary care center and does not represent the surrounding community or rural areas. Definitive diagnoses could rarely be established due to the lack of appropriate laboratory testing and equipment such as MRI, EEG, and EMG that is either too expensive to purchase or maintain. More importantly, there is likely a large amount of neurological disease goes unrecognized because of generalized lack of neurological expertise.

Additionally, the exact number of HIV⁺ individuals is unknown. The actual number is likely higher as only small percentage of the general population actually had undergone HIV testing. Patients often refuse testing due to the stigma associated with HIV/AIDS. The prevalence rate for the country is 15.2% among adults age 15–49 yo.¹³ It is higher among women (18%) than among men (13%) and considerably higher in urban populations (25–35%) than in rural populations (8–16%).¹⁴ Therefore, it is likely that we have underestimated the number of HIV⁺ patients in our cohort.

There may be an overrepresentation of movement disorders in the outpatients as this is the specialty area of the examining neurologist who follows these patients out of academic interest. Patients were classified to a single diagnostic category based on their symptoms, exam findings, and testing. However, certain conditions arguably fit into multiple diagnostic categories such as HIV dementia or transverse myelitis. The statistical analysis conducted was planned *a priori*. Given the exploratory nature of this work, no p-value adjustments were made for multiple comparisons.

This study does have the advantage of relying on the exam findings of a trained neurologist as opposed to a chart review where neurological findings and conditions can easily be missed by a non-neurologist. It provides contrast in terms of how inpatient and outpatient neurological disease differs in the HIV/HAART era in an urban third world setting. Infectious diseases are the most common inpatient neurological illness while non-infectious neurological illnesses are most prominent among outpatients. This study also illustrates that there is still a setting where the neurological exam is the most useful diagnostic tool.

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Table 1

Hospital-based studies of neurological disorders in sub-Saharan Africa

Country	No. of cases	Source	Study design	Diagnosis
Nigeria	9600	Osuntokun et al., 1970	Retrospective chart review of adult and pediatric medical inpatients and outpatients with neurological disease from 1957–1969.	Infectious 43% Epilepsy 7% Vascular disease 6%
Tanzania	937	Matuja et al., 1989	Cross-sectional study of adult neurological admissions over 12 months.	Infectious 38% Vascular disease 32% Spinal Cord disease 9% Seizure d/o 6% Neuropathies 5% Intracran. tumors 4%
Kenya	~ 12000*	Kwasa et al., 1992	Retrospective chart review of neurological disease from adult medical inpatients and outpatients from 1978–1987	Meningitis 23.1% Epilepsy 16.6% CVD 15%
Zambia	186	Birbeck, 2001	Cross-sectional study of adult and pediatric neurological admissions at a rural hospital over 13 weeks.	Febrile convulsions 27% Neuropathy 23% CNS infections 17% Epilepsy 16% Stroke 9%
Ethiopia	147	Bowers et al., 2007	Retrospective chart review of adult neurological admissions at an urban hospital over 6 months	Meningitis/meningo-encephalitis 19.7% Delerium/coma 17.0% Hemiparesis 34.7% Para-/tri/quadruparesis 17.0% Seizure 6.1%
Ethiopia	141	Bowers et al., 2007	Retrospective chart review of adult neurological admissions at a rural hospital over 6 months	Meningitis/meningo-encephalitis 20.1% Delerium/coma 30.5% Hemiparesis 28.4% Para-/tri/quadruparesis 13.5%
Tanzania	340	Winkler et al., 2009	Prospective study of adult and pediatric admissions with a neurological diagnosis in a rural hospital over 8 months. – without diagnostic uncertainties.	Febrile convulsions 24% Meningitis 22% Epilepsy 19% Cerebral Malaria 15% Pott's disease 6%
Tanzania	318	Winkler et al., 2009	Prospective study of adult and pediatric admissions with a neurological diagnosis in a rural hospital over 8 months – with minor diagnostic uncertainties.	Myelo-/radiculo-/plexo-/polyneuropathy 19% Head trauma with neuro impairment 17% Seizures 15% Non-infectious encephalopathy 14% CVA 10%

* Total number of patient was not overtly stated in the text but could be extrapolated from prevalence data.

Table 2

Patient demographics and prevalence of HIV infection

	Inpatients	Outpatients
Number	443	368
Age median (range)	39 (10–85)	39 (15–80)
Men	219 (49.4%)	168 (45.6%)
HIV +	31 (14.2%)	37 (22.0%)
HIV –	4 (1.8%)	11 (6.6%)
Untested	184 (84.0%)	120 (71.4%)
Women	224 (50.6%)	200 (54.3%)
HIV +	36 (16.0%)	21 (10.5%)
HIV –	7 (3.0%)	13 (6.5%)
Untested	181 (81.0%)	166 (83.0%)
Total HIV⁺	67 (15.1%)	58 (15.8%)

Table 3Neurological diseases among HIV⁺ and general inpatients

Inpatient Diagnostic Categories	HIV+		General		P-value
	no.	%	no.	%	
Infectious	26	38.8	47	12.5	<0.0001
Neuropathy/Radiculopathy	10	14.9	37	9.8	0.20
Cerebrovascular disease	6	8.9	62	16.5	0.14
Myelopathy	5	7.5	10	2.7	0.06
Dementia/Neurodegenerative	4	6.0	15	4.0	0.5
Encephalopathy	4	6.0	14	3.7	0.33
Demyelinating	3	4.4	11	2.9	0.45
Movement disorders	3	4.4	25	6.6	0.78
Seizures/Epilepsy	2	3.0	27	7.2	0.28
Neoplasm/Neoplastic process	2	3.0	19	5.1	0.75
Subarachnoid hemorrhage	1	1.5	6	1.6	1
Neuromuscular	0	0.0	16	4.2	0.14
Headache/Cephalgias	0	0.0	11	2.9	0.38
Trauma	0	0.0	9	2.4	0.36
Herpes zoster neuralgia	0	0.0	7	1.9	0.6
Psychiatric disorders	0	0.0	7	1.9	0.6
Spastic Paraparesis	0	0.0	7	1.9	0.6
Cervical spondylosis	0	0.0	6	1.6	0.59
Diagnosis unclear	1	1.5	16	4.2	
Other conditions	0	0.0	24	6.4	
Total	67		376		

Table 4Neurological diseases among HIV⁺ and general outpatients

Outpatient Diagnostic Categories	HIV+		General		P-value
	no.	%	no.	%	
Neuropathy/Radiculopathy	18	31.0	43	13.8	0.003
Cerebrovascular disease	8	13.8	18	5.8	0.04
Dementia/Neurodegenerative	8	13.8	9	2.9	0.002
Encephalopathy	7	12.1	4	1.3	0.04
Headache/Cephalgias	4	6.9	60	19.4	0.022
Myelopathy	4	6.9	1	0.3	0.002
Seizures/Epilepsy	1	1.7	39	12.6	0.01
Neuromuscular	1	1.7	12	3.9	0.7
Infectious	1	1.7	7	2.3	1
Neoplasm/Neoplastic process	1	1.7	7	2.3	1
Demyelinating	1	1.7	5	1.6	1
Movement disorders	0	0.0	47	15.2	0.0003
Psychiatric disorders	0	0.0	11	3.5	0.22
Fibromyalgia	0	0.0	9	2.9	0.36
Cervical Spondylosis	0	0.0	8	2.6	0.36
Spastic Paraparesis	0	0.0	4	1.3	1
Diagnosis unclear	4	6.9	4	1.3	
Other conditions	0	0.0	22	7.1	
	58		310		