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Electrodiagnostic consultations in Zambia: Referral characteristics and neuromuscular disorders

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ABSTRACT

Introduction: Research on neuromuscular disorders in sub-Saharan Africa is scarce. We aimed to delineate referral characteristics and the neuromuscular disorders observed among electrodiagnostic (EDX) consultations in a tertiary care setting in Zambia.

Methods: EDX records were reviewed for all specialist-performed studies after the establishment of the laboratory. The frequency of demographic, medical characteristics, and final EDX impressions are presented.

Results: Among 108 referrals, 52% were male, 84% were adults (mean age 44 years). Referrals were predominantly outpatients (85%) and sent by neurologists (68%). HIV infection was common (12%). Diabetes was rare (3%). Overall, 77% of studies were abnormal. Polyneuropathy was the most common abnormal EDX finding, followed by motor neuron disease.

Discussion: A diverse range of neuromuscular diseases was evaluated among EDX referrals in Zambia. Though labor and expertise intensive, access to EDX consultation can enhance clinical care and facilitate research and surveillance of neuromuscular disorders in the region.

1. Introduction

Neuromuscular disorders are an especially underrepresented area of research in sub-Saharan Africa (SSA), even though neurological disorders in general contribute substantially to disability and mortality in this environment [1]. Retrospective and prospective studies of neurology consultations from the region suggest a high burden of neuromuscular disorders exists, contributing to between 13.6 and 27.6% of all adult inpatient and outpatient neurological consultations in both urban and rural settings [2–7]. Unfortunately, these studies lack diagnostic specificity and commonly combine neuromuscular disorders into localization-related categories like plexus and nerve disorders, radiculopathy, or muscle/neuromuscular junction disorders, rather than delineating specific clinical entities with diverse public health, health policy planning, prognostic, and treatment implications. Among pediatric neuromuscular disorders, data on acute flaccid paralysis (AFP) are available from the World Health Organization-led Polio Global Eradication Initiative, which surveils poliomyelitis cases in children under age 15 years in the sub-continent, but the etiologies and electrophysiologic profile of non-polio AFP remain poorly defined [8]. Very little is known about other pediatric neuromuscular disorders outside of a handful of retrospective studies of outpatient clinic consultations and small disease-specific case series. We found only three small case series studies reporting evaluations with nerve conduction

Abbreviations: AFP, Acute Flaccid Paralysis; ALS, Amyotrophic Lateral Sclerosis; DSP, Distal Symmetric Polyneuropathy; EDX, Electrodiagnostic; GBS, Guillain-Barré Syndrome; NCS/EMG, Nerve Conduction Studies/Electromyography; MND, Motor Neuron Disease; SMA, Spinal Muscular Atrophy; SSA, sub-Saharan Africa; SPSS, Statistical Package for the Social Sciences; UTH, University Teaching Hospital

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studies/electromyography (NCS/EMG) [6,9,10]. Understanding the epidemiology of neuromuscular diseases seen in low- and middle-income countries is needed for appropriate public health guidelines and resource allocations. Limited neurologic expertise and diagnostic capacity are considerable barriers to neuromuscular disease care and research in the region. Since 2012, we have established the first electromyography laboratory in Zambia for research and clinical purposes. In this article, we offer a rare window into the spectrum of neuromuscular diseases presenting for electrodiagnostic (EDX) consultation in a tertiary care setting in SSA and explore the challenges and benefits of expanding access to EDX consultations in this setting.

2. Methods

2.1. Population

All NCS/EMG were performed at the University Teaching Hospital (UTH) in Lusaka, Zambia. UTH is an 1800 bed teaching hospital and the only tertiary care center in Zambia, a country of 15 million citizens. Additional available neurodiagnostic assessments include magnetic resonance imaging, computed tomography, and electroencephalography. We present EDX consultations conducted between March 17, 2015 and November 14, 2017, during which period the lab is open approximately 9 months annually. Referrals were accepted from any inpatient or outpatient physician or facility, including private practice in this time frame. Fees are waived for those who could not afford testing and thus, direct cost was not a barrier to the study.

2.2. Electrodiagnostic consultation

For each EDX consultation, a neurological consultation with a complete neurological examination is performed, followed by performance of both NCS and EMG by a fellowship-trained clinical neurophysiologist (MK). One Xltek Neuromax electromyography unit was utilized for all consultations. In the absence of local normative data during the period reported in this study, all NCS/EMG were interpreted using normative data from U.S. populations or intra-person and/or intra-limb comparisons in cases in which side-to-side asymmetries were notable [11]. During this period, limb temperatures were documented in all cases and, when necessary, a standard conversion of 0.2 milliseconds per degree below 32 degrees Celsius was utilized to correct sensory peak latencies and compound motor action potential distal onset latencies. EDX data and any technical limitations were interpreted in the context of clinical history, neurological examination, and any available adjunctive investigations to formulate a final electroclinical impression.

2.3. Primary outcomes

Referral logs were reviewed for all cases performed during the period of interest. We reviewed HIV status, history of tuberculosis treatment, history of alcohol abuse, and the final electroclinical diagnosis. As participants often arrived without medical files, especially from pediatric and private referral sources distant from the adult hospital and clinic block, we were unable to consistently document the referring provider impression for comparison to the final electroclinical diagnosis. Abstracted de-identified data was analyzed using SPSS 22. The frequency (%) of adult and pediatric referrals, referral source, and medical characteristics are presented. We also report the frequency (%) of EDX localizations and the final electroclinical impressions for adult and pediatric referrals from the final reports.

3. Results

Demographic and medical characteristics of patients referred for NCS/EMG are presented in Table 1. Briefly, 91 (84%) referrals were ≥ 18 years of age and 56 (52%) were male. Twenty-four (22%) were known to be HIV positive, 51 (47%) were HIV negative, while an additional 33 (31%) did not have documentation of HIV status available at the time of the consultation. Prior history of isoniazid exposure was reported by 12 (11%) patients, and a history of alcohol abuse was documented in 6 (6%) patients. Diabetes was an uncommon comorbidity among referrals with only 3 (3%) reporting a history of diabetes. Referral source is outlined in Table 2. The majority of referrals came from providers within UTH and most were referred by the neurology division within the Department of Internal Medicine. Overall, 83 (77%) referrals had abnormal NCS/EMG.

Table 1
Demographic & clinical characteristics of 108 electrodiagnostic referral.

	n (%)
Female sex	52 (48%)
Adult	91 (84%)
Mean age, yrs, (range)	43.5 (18–77)
Median age, yrs, (IQR)	41 (22)
Pediatric	17 (16%)
Mean age, yrs, (range)	7.1 (18 months-17 yrs)
Median age, yrs, (IQR)	5 (9.8)
Outpatient	92 (85%)
Abnormal NCS/EMG	83 (77%)
HIV status	
HIV+	24 (22%)
HIV-	51 (47%)
Unknown	33 (31%)
History of isoniazid exposure	
Yes	11 (11%)
No	79 (73%)
Not recorded	17 (16%)
History of diabetes	
Yes	3 (3%)
No	96 (89%)
Not recorded	9 (8%)
History of alcohol abuse	
Yes	6 (5%)
No	86 (80%)
Not recorded	16 (15%)

3.1. Adult referrals

Table 3 provides the frequency of findings by electrophysiologic localization for all patients 18 years or older. Polyneuropathies were the most common abnormal EDX finding, accounting for 23 (25%) adult referrals. Distal symmetric polyneuropathy (DSP) was the most common diagnosis ($n = 10$; 11%) with NCS/EMG demonstrating a length-dependent axonal sensory or sensorimotor polyneuropathy. HIV and vitamin B12 deficiency were the most commonly identified risk factors. Three (3%) referrals received an electroclinical diagnosis of a suspected hereditary polyneuropathy, including one predominately demyelinating sensorimotor, and two predominately axonal sensorimotor electrodiagnostic characterizations. Immune-mediated polyneuropathies included three (3%) patients meeting clinical and EDX

Table 2
Source of electrodiagnostic referrals[†].

	N (%)
Adult neurology clinic	61 (57%)
Pediatric neurology clinic	12(11%)
Internal medicine	20(19%)
Neuro/orthopedic surgery	4(4%)
Physiotherapist	1(1%)
Private referral	9(8%)

[†] $n = 107$, one EMG without documented referral source.

Table 3
Primary Electrodiagnostic Localization of Adult EMG Referrals by HIV status.

	HIV- (*n* = 45)	HIV + (*n* = 22)	Unknown (*n* = 24)	Total (*n* = 91)
Radiculopathy	1 (2.2%)	0 (0%)	6 (25.0%)	7 (7.7%)
Polyradiculopathy	4 (8.9%)	4 (18.2%)	1 (4.5%)	9 (9.9%)
Motor neuron disease	8 (17.8%)	3 (13.6%)	0 (0%)	11 (12.1%)
Plexopathy	0 (0.0%)	0 (0.0%)	3 (12.5%)	3 (3.3%)
Mononeuropathy	3 (6.7%)	2 (9.1%)	4 (16.7%)	9 (9.9%)
Polyneuropathy	12 (26.7%)	7 (31.8%)	3 (12.5%)	23 (25.2%)
Neuromuscular junction	1 (2.2%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
Myopathy	1 (2.2%)	1 (4.5%)	0 (0.0%)	2 (2.2%)
Normal	13 (28.9%)	5 (22.7%)	6 (25.0%)	24 (26.4%)
Other	1 (2.2%)	0 (0.0%)	1 (4.2%)	2 (2.2%)

criteria for chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). Among these, one case was consistent with multifocal acquired demyelinating sensory and motor neuropathy (MADSAM). One (33%) CIDP case was HIV positive. A pure sensory neuronopathy was seen on NCS/EMG in one (1%) referral.

Six (7%) referrals were for acute polyneuropathies, including four (4%) cases of Guillain-Barré Syndrome (GBS). Electrophysiologic profiles were varied including one demyelinating sensorimotor polyradiculoneuropathy, two sensorimotor polyradiculoneuropathy with mixed demyelinating and axonal features, and one acute motor axonal neuropathy. Two (2%) additional cases had acute axonal sensorimotor polyneuropathy, which included one nutritional (1%) and one (1%) patient with intentional toxic ingestion.

EDX consultations revealed disorders of the motor neuron in 11 (12%) adult referrals. In one (1%) referral, a polio- or poliomyelitis-like illness was suspected. Ten (11%) cases were consistent with amyotrophic lateral sclerosis (ALS), including two clinically definite, five probable, and one possible ALS case by the revised El Escorial Criteria [12]. Two of these cases presented with ALS variants, including one HIV + patient with brachial amyotrophic diplegia and one HIV negative patient with progressive muscular atrophy. Among ALS and ALS variants, cases were predominantly male (*n* = 8; 80%) and had a mean age at the time of examination of 53.3 years (range 40–73 years). Limb onset was the most common clinical presentation (*n* = 7; 70%). Three (30%) cases were retroviral-associated.

Polyradiculopathies were identified on NCS/EMG in 9 referrals (9%), including four (4%) patients with acute bilateral lumbosacral polyradiculopathies and three (3%) referrals with severe acute or subacute polyradiculopathies involving both the cervical and lumbosacral regions. Two (2%) additional cases were noted to have chronic lumbosacral polyradiculopathies.

Single or multilevel acute, subacute, and chronic radiculopathies of suspected degenerative etiologies, such as disc herniation, were confirmed by EDX studies in another seven referrals (8%), including six (6%) cervical radiculopathies and one (1%) with unilateral lumbosacral radiculopathy.

Brachial plexus abnormalities were found in 3 (3%) referrals. Etiologies included infiltrative and/or radiation-induced, and traumatic with mixed nerve root avulsions. No lumbosacral plexopathies were identified.

Mononeuropathies were diagnosed in 9 (10%) referrals. Lacerations and traumatic injuries were equally as common as mononeuropathies at compressive sites. Traumatic injuries included one median recurrent motor branch injury, and two radial nerve injuries. One sciatic neuropathy in the setting of prior hip replacement surgery was also found. Focal entrapment mononeuropathies were seen in four (4%) referrals, including three with carpal tunnel syndrome, one of which also had evidence of ulnar neuropathy at the elbow. One compressive radial nerve injury at the spiral groove was also seen.

Myopathy was diagnosed in two (2%) referrals, including one inflammatory myopathy and another of unclear etiology.

Table 4
Electrodiagnostic Localization of Pediatric Referrals by HIV Status.

	HIV- (*n* = 6)	HIV + (n = 2)	Unknown (n = 9)	Total (*n* = 17)
Motor Neuron Disease	4 (66.7%)	0 (0%)	3 (33.3%)	7 (41.2%)
Polyneuropathy	0 (0%)	1 (50%)	2 (22.2%)	4 (23.5%)
Normal	1 (16.7%)	1 (50%)	3 (33.3%)	5 (29.4%)
Other*	1 (16.7%)	0 (0%)	0 (0%)	1 (5.9%)

* Facial Diplegia.

The remaining (1%) abnormal EDX study included NCS/EMG evidence of continuous motor unit activity and history and examination consistent with stiff person syndrome.

Twenty-four (26%) referrals had normal EDX studies. Among these nearly half (*n* = 12) were referred with complaints of unilateral or bilateral limb pain or paresthesias with normal neurological examinations. Two referrals for evaluation of dysphagia and/or dysphonia of unknown etiology had normal EDX evaluations. Three (3%) were referred for myasthenia gravis evaluation and one (1%) for myopathy. Seven (8%) referrals were found to have an etiology not related to a peripheral nervous system disorder including a case of left foot dystonia, hydrocephalus, cerebellar disorders, and thalamic and basal ganglia stroke.

3.2. Pediatric referrals

The most common neurophysiologic diagnosis among pediatric referrals (Table 4) were disorders of the anterior horn cell (*n* = 7, 41%). One case of anterior horn cell disease was clinically suspected to be a polio- or poliomyelitis-like illness and the remaining six (35%) referrals the electrodiagnosis pointed to spinal muscular atrophy (SMA). Five referrals followed a clinical course most consistent with SMA type II, while the remaining case appeared consistent with SMA type III. None of these cases reported a similarly afflicted family member.

Polyneuropathies were diagnosed in four (24%) teenagers. Two (12%) cases were consistent with a subacute to chronic length-dependent axonal sensorimotor polyneuropathy and in one HIV positive patient, there was also clinical evidence of a myeloneuropathy. GBS versus a toxic etiology was entertained in an 18-month-old with findings of an acute to subacute length-dependent sensorimotor polyneuropathy with mixed axonal and demyelinating features. One (6%) case of facial diplegia was also referred, but had an incomplete EDX study due to poor tolerance for the test.

4. Discussion

The compendium of neuromuscular disorders seen in our study is in contradistinction to many studies from other world regions where entrapment neuropathies and lumbar radiculopathies are among the most common suspected and confirmed diagnosis amongst EDX referrals [13–18]. A few studies, including a study of seven European tertiary care centers, found polyneuropathy as the commonest EDX abnormality among EMG referrals, but did not report the etiologies of polyneuropathies among them [16,18,19]. In our referral series, NCS/EMG facilitated diagnosis of both acute and chronic immune-mediated polyneuropathies. As corticosteroids, plasmapheresis and intravenous immunoglobulins are available at the University Teaching Hospital, accurate and expedient diagnosis are of paramount importance. Surveillable cases of acute flaccid myelitis were also seen. Leprosy cases were notably absent among our polyneuropathy and polyradiculopathy cases. Leprosy programs in Zambia reported steady declines in new leprosy case identification from 2.73 cases/10,000 in 1991 to 0.43 cases/10,000 population in 2010, but data on the geographical distribution of cases within Zambia are not available [20]. We suspect that

reduced case finding efforts within SSA and/or an urban referral bias for this largely rural disease may also be contributing factors for absence of leprosy cases among our early referrals. There may be regional or district-level clusters, similar to those seen in other endemic countries not captured during the early period of EDX availability in Zambia with limited regional knowledge of access to this test outside of Lusaka [21–24].

We found no EDX studies reporting similar high rates of MND [16,18,19]. ALS cases in our referral series were more likely to be male and to have limb-onset, similar to U.S. populations, but were slightly younger and were frequently HIV-associated. A heightened risk of MND has been seen in HIV populations in the U.S., but has not been previously studied in HIV populations from SSA [25,26]. Facilitating study in populations from SSA with unique genetic diversity and distinct infectious and environmental exposures may be highly informative in understanding the complex pathophysiology of ALS.

The overall rate of abnormal EDX studies of 77% in our study is similar to most prior studies with rates ranging from as low as 45% amongst referrals in a community setting in Italy to as high as 80% in other tertiary care settings. We did not identify prior EDX referral studies reporting the prevalence of diabetes, HIV, or other common comorbidities associated with peripheral nerve disorders. The high prevalence of HIV and low prevalence of diabetes in our NCS/EMG series is reflective of population-based prevalence estimates of 13% for HIV infection and 2.7% for diabetes in Zambia [27,28]. A lead-time or other bias may exist in our study wherein patients previously living with chronic neuromuscular disorders without access to EDX consultation were referred earlier when testing became available. We anticipate that the frequency of specific neuromuscular diseases seen in our laboratory will continue to change over time, as word-of-mouth increases knowledge of test availability in Zambia.

Several limitations should be noted. The lack of normative NCS/EMG data in our population and absence of limb warming capacity raises difficulties in interpretation of EDX studies in our referral series. However, all studies were interpreted with acknowledgment of these limitations and were performed as an extension of the clinical history and neurological examination. We have since added a limb warming protocol in our laboratory and are in the process of developing normative values in HIV negative community controls for research and clinical purposes. Rare studies reporting normative NCS data in African, Asian and Middle Eastern populations have not found consistent differences in NCS thresholds for normality compared with those from other world regions [29–33]. The high prevalence of HIV among our population will require additional consideration as well. NCS findings may be more variable in HIV infection, similar to findings seen in median mononeuropathy at the wrist in patients with diabetes [34]. However, the impact of HIV infection on NCS has not been adequately studied [35–38].

Despite such limitations, our experience suggests that EDX referrals from a range of medical referral sources are highly appropriate and lead to identification of a diverse range of neuromuscular disorders with improved diagnostic specificity in a tertiary care setting in Zambia. Since both symptomatic and disease-modifying treatments are available on government health facility formularies in Zambia, the EDX consultation is highly useful for clinical management of neuromuscular disease in this environment. While we were not able to objectively assess the impact of the EDX consultation on subsequent clinical decision-making and patient outcomes, others have demonstrated significant improvements in patient outcomes in other populations when EDX findings are abnormal [15,39,40]. In our study, referrals with normal neurologic examinations also commonly had normal NCS/EMG. This has been demonstrated in other populations as well and suggests that EDX consultation has more limited diagnostic utility in patients with normal neurological examinations, perhaps with the exception of carpal tunnel syndrome [13,17]. These observations are important in resource-constrained settings and can reduce wait times and maximize availability of the test for those who are most likely to benefit from EDX consultation.

Neurodiagnostic capacity-building in resource-constrained settings is a challenging undertaking. One NCS/EMG machine and one subspecialist physician for NCS/EMG performance result in limited access to EDX and may result in referral bias wherein more severe indications are more likely to be referred and seen. Due to lack of local neuromuscular expertise, we have also found it necessary to allot additional time for patient counselling and management recommendations as a standard part of the EDX consultation. Task-shifting or algorithmic approaches are needed, but not as easily constructed for EDX consultation as for other neurodiagnostic modalities. Such strategies have been implemented for some specific conditions such as carpal tunnel syndrome and DSP in other settings [13,41].

Our referral series is the first reported from SSA and is useful for EDX guideline development and capacity-building activities for others in similar environments. The diverse spectrum of neuromuscular disease seen highlight the need for improvements in clinical care, research and existing outbreak surveillance programs in the region. Opportunities for task redistribution or development of standardized screening protocols, perhaps under specialist supervision must be considered. This will be a challenging endeavor based on prior experience from other world regions [42–46]. However, facilitating clinical care and research on neuromuscular disorders in SSA is long overdue.

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