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Multiple sclerosis in Kenya: Demographic and clinical characteristics of a registry cohort

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Abstract

Background: Multiple Sclerosis (MS) is the leading cause of non-traumatic neurological disability in young adults. There is limited literature regarding the burden of MS in sub-Saharan Africa (SSA).
Objective: To describe the demographic and clinical characteristics of patients with MS (PwMS) presenting to a tertiary referral hospital in Nairobi.
Methods: We conducted a retrospective descriptive study for PwMS presenting to Aga Khan University Hospital, Nairobi from 2008–2018.
Results: 99 cases met the diagnostic criteria for MS with a male to female ratio of 1:4. Majority (68.7%) of PwMS were indigenous Africans with a mean age of onset of 30.7 years. Mean duration from symptom onset to first neuro-imaging was 5.04 years. Only 33% of patients had sensory symptoms at onset whereas 54.5% had vitamin D deficiency/insufficiency. Majority (79.5%) had relapsing remitting MS (RRMS) and 56.6% were initiated on disease modifying therapy (DMT). Only 21.2% of patients on DMT were non-compliant. Patients with RRMS were more likely to be initiated on DMT at our hospital ($p < 0.001$).
Conclusion: Clinical characteristics of these patients largely resemble those of other SSA cohorts and African American patients. There was a delay between symptom onset and neuroimaging. There were also issues with DMT compliance.

Keywords: Multiple sclerosis, Kenya, Nairobi, epidemiology, clinical, profile, Sub-Saharan Africa

Introduction

Multiple Sclerosis (MS) is the leading cause of progressive neurological disability in young adults[1] and has a huge impact on functional and financial aspects of life.[2] It is the most common immune-mediated inflammatory demyelinating disease of the central nervous system (CNS). The prevalence of MS is high in Northern Europe, North America and Australia. Recent data have questioned the conventional thinking of MS being more prevalent at higher latitudes, with rising reports of MS morbidity from regions with previously low prevalence.

MS seems to have a different phenotype depending on race. For example, in one study, African Americans were found to experience earlier onset and faster disease progression than white Americans.[3] However, these differences were overestimated when there was no adjustment for socioeconomic factors. There have also been studies demonstrating greater inflammatory activity within the cerebrospinal fluid[4] and more exacerbations in African Americans compared to Caucasian Americans with MS.[5] There is little epidemiological evidence of the MS phenotype in Africa and therefore it is difficult to ascertain whether it would be similar or different to that described in the same racial groups outside Africa.

In Kenya, there have only been 2 published MS case series, totaling 15 patients.[6,7] These patients were

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mainly female indigenous Africans, and usually presented with visual or sensory disturbances, but otherwise their disease progression and therapeutic interventions were not evaluated. We have previously described 29 MS cases from a diagnostic audit at our centre.[8] We therefore set out to collect all the cases of MS known to our hospital and describe the findings here.

Materials and methods

Study setting
We conducted a descriptive study based on medical records of MS patients from January 2008 to December 2018 at the Aga Khan University Hospital, Nairobi (AKUHN) and other sources from affiliated neurologists (including neurologists in private practice).

The study was approved by the Institutional Ethics Review Board at AKUHN.

Case finding
We identified MS cases through (Figure 1):

(i) Medical record coding: our institution uses the International Classification of Diseases (ICD-10) coding system and we applied the G35 heading code for MS and all sub-codes to identify cases.

(ii) Pharmacy: we searched for patients who had the following drugs and disease modifying therapies (DMTs) prescribed, which are the only ones available in the country: interferon beta-1a, glatiramer acetate, natalizumab, rituximab, intravenous methylprednisolone (IVMP), and azathioprine.

(iii) Laboratory: patients who had ever undergone testing for cerebrospinal fluid oligoclonal bands (CSF OCBs).

(iv) Neurophysiology: all patients who had had visual evoked potentials (VEP).

(v) MS databases held by neurologists in the hospital.

The cases identified from the above steps were collated and MS diagnoses then confirmed or rejected based on the modified McDonald's criteria.[9] Neuro-imaging including magnetic resonance imaging (MRI) could only be done after identifying cases through the above steps as our electronic data management and radiology reporting/archiving systems do not have indexing mechanisms to allow searching for particular keywords pertinent to MS. We excluded patients who were suspected to have MS but did not have complete evaluation and therefore did not meet the diagnostic criteria.

Data collection, management and analysis
We captured demographic variables (date of birth, age, gender, race, marital status, migration status, occupation), MS subtype [relapsing-remitting MS (RRMS), primary progressive MS (PPMS) or
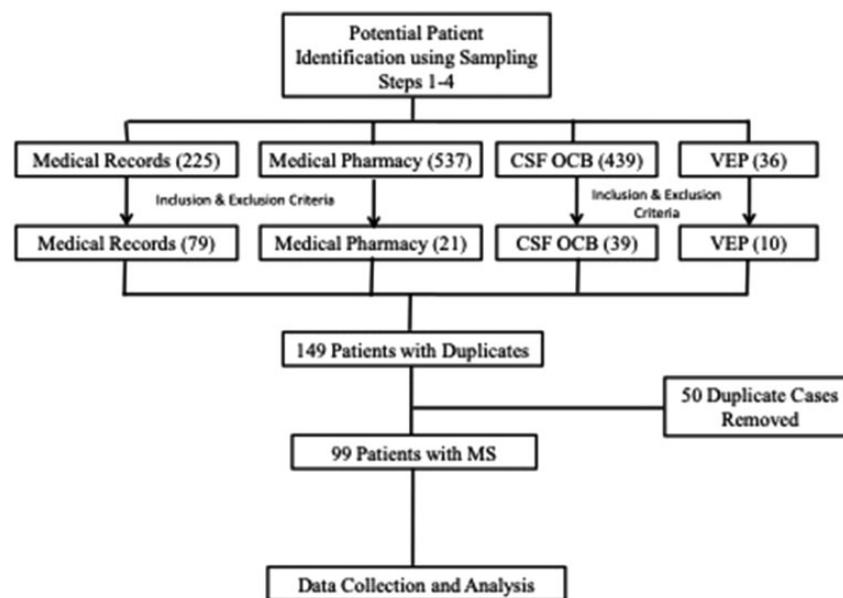

Figure 1. Potential patient identification using sampling steps 1–4.

secondary progressive MS (SPMS)],[10] symptoms at presentation, comorbidities, and current as well as previous medications, including DMTs. Important dates recorded included date of onset of symptoms, date of diagnosis, date of each documented relapse and/or admission, date of the first clinic visit/admission at AKUHN (Visit 1), date of every MRI of the CNS, and duration of DMT use. If available, we recorded the expanded disability status scale (EDSS)[11] scores from the clinic notes.

The data were recorded in the form of an electronic database and encrypted with a password which was only known to the investigators. Categorical variables were expressed as frequencies and percentages, continuous variables were expressed as means and standard deviations. Univariate analysis was utilized using the Chi Square (χ^2) or the Fisher's Exact test for DMT initiation in RRMS patients based on in hospital or outside hospital and the Student's t-test or non-parametric equivalent tests for comparison of EDSS scores between the first and last visit, RRMS relapses per year based on pre-DMT vs post first DMT, and time to first relapse according to the type of MS. Normality of the continuous variables was determined by the Shapiro Wilk test. Correlation tests were performed using Spearman's Correlation test to associate factors with MS groups. A p value of less than 0.05 was considered statistically significant. Data analysis was conducted using IBM SPSS statistical software (Version 20).

Results

Patient characteristics
We identified 99 patients with MS between 2008-2018. Majority (79.8%) of the patients (n = 79/99) were female, giving a male-to-female ratio of 1:4, and 70.1% of patients (n = 68/99) were indigenous black Africans (Table 1). The mean age of symptom onset was 30.77 years [standard deviation (SD) = 10.03], while the mean age at diagnosis was 34.19 years (SD = 11.36) (Table 1). Majority (78.4%) of the patients (n = 69/99) were employed and working. Most of our patients had RRMS (79.6%, n = 78/99). More than half (54.5%) of the patients (n = 54/99) were diagnosed with MS when they came to AKUHN, with the rest having their diagnosis made elsewhere. The mean duration of symptoms prior to diagnosis was 3.94 years (SD = 6.82).

About 61.6% of patients (n = 61/99) had at least one comorbid condition, the most common being Vitamin D insufficiency/deficiency (Table 1). Approximately 20% of our patients (n = 20/99) suffered from a psychiatric condition, most commonly depression. Two patients had suffered from avascular necrosis of the hip(s) (See supplementary material for more information).

Clinical features
One-third (33.3%) of the symptoms at onset were sensory in nature, while 29% had optic neuritis at onset (Figure 2). 34% of patients (n = 34/99) had 2 or more of the following features at onset: sensory symptoms; weakness; optic neuritis; ataxia and vertigo; and Cranial nerve palsy. These symptoms were also usually the same presenting features when the patient first made contact with AKUHN, although urinary symptoms were also more common (present in 26.3% and 17.2% respectively). The mean duration between the first and second visit to AKUHN was 7.8 months (SD = 16.5). More than half (64.3%) of the patients (n = 63/99) who presented to AKUHN had a relapse and 52% (n = 51/99) were first seen in the inpatient setting (Table 1). EDSS scores were not reported within any of the clinic notes.

Investigations
More than half (53%) of patients (n = 52/99) had their first MRI prior to first visiting AKUHN, of which 42% (n = 22/52) had enhancing lesions. The mean duration from symptom onset to obtaining the first MRI of the CNS was 5.04 years (SD = 8.01) (Table 1). Majority of the patients (91%; n = 41/45) who had their first MRI at AKUHN had enhancing lesions. Among patients who had their first MRI prior to visiting AKUHN, 41% (41/52) met the radiologic criteria of MS. Among patients who had their first MRI at AKUHN, 82% (37/45) met the radiologic criteria of MS.

During diagnostic evaluation, 63% of patients (n = 63/99) had CSF studies done, of which 39 patients were positive for CSF OCBs (as indicated by an elevated IgG level in CSF of more than 34 mg/l). There were no abnormalities in CSF white cell counts and no organisms isolated in CSF culture. All 45% of patients (n = 45/99) had VEPs done, of which 20 were abnormal. A total of 7 patients were evaluated for John Cunningham virus (JCV) antibodies, of which 3 were positive, all of whom were on natalizumab or rituximab.

Admissions and relapses
The mean number of visits to AKUHN was 8.29 (SD = 8.84), while the mean number of admissions

Table 1. Demographic characteristics of MS patients (n = 99 unless otherwise stated).

Gender	Male	20	20.20%
	Female	79	79.80%
Race (n = 97)	African	68	70.10%
	Asian	16	16.49%
	Other	13	13.40%
Occupation (n = 88)	Working	69	78.41%
	Retired	6	6.82%
	Student (in school = 6)	12	13.64%
	Unemployed	1	1.14%
Family history of MS		5	5.10%
Comorbidities	Vitamin D deficiency/insufficiency	54	54.55%
	Psychiatric illness	20	20.20%
	Others		
	Neurological/MS-related	17	17.17%
	Urologic	7	7.07%
	Migraine	4	4.04%
	Steroid-induced diabetes	2	2.02%
	Avascular necrosis of the hip	2	2.02%
	Seizures	2	2.02%
	Non-neurological	82	82.82%
Age at diagnosis (n = 98) [mean ± SD]		34.19 (±11.36)	
Age at onset of symptoms (n = 91) [mean ± SD]		30.77 (±10.03)	
Types of MS (n = 98)	Relapsing-remitting MS	78	79.59%
	Secondary progressive MS	15	15.31%
	Primary progressive MS	4	4.08%
	CIS	1	1.02%
Years from onset to diagnosis (n = 91) [mean ± SD]		3.94 (±6.82)	
Years from symptom onset to first MRI (n = 85) [mean ± SD]		5.04 (±8.01)	
CSF OCB (n = 63)	Negative	24	38.10%
	Positive	39	61.90%
VEP Result (n = 45)	Normal	24	53.33%
	Abnormal	20	44.44%
	Inconclusive	1	2.22%
Vitamin D levels (n = 99)	Normal[a]	16	16.16%
	Insufficient[b]	29	29.29%
	Deficient[c]	25	25.25%
Vitamin B12 deficiency (n = 65)		3	4.62%
JCV[d] Antibodies (n = 7)	Negative	4	57.14%
	Positive	3	42.60%
RRMS relapses/year	PreDMT	0.90 (±0.93)	p = 0.042[f]
	Post First DMT	0.59 (±0.60)	
Time to first relapse[e]	RRMS (n = 70)	3.25 (±6.29)	p = 0.005[f]
	SPMS (n = 8)	10.43 (±7.15)	

[a]Normal Vitamin D: $\geq$ 30 ng/mL.
[b]Vitamin D insufficiency: 20–29.9 ng/mL.
[c]Vitamin D deficiency: < 20 ng/mL.
[d]JCV: John Cunningham Virus.
[e]Relapse data for SPMS relates to relapses that occurred prior to progression of MS.
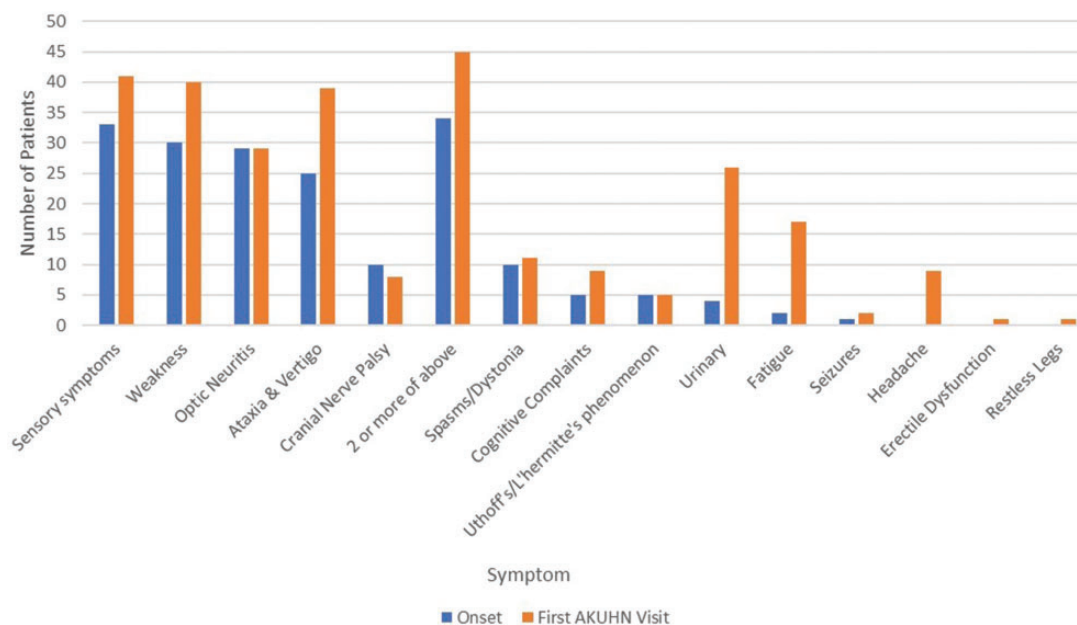[f]Statistically significant (p<0.05).

Figure 2. Symptoms at onset and at the first AKUHN visit.

during the study period was 1.85 (SD = 2.27). The mean duration to first relapse was 3.99 years (SD = 6.66). The most common reason for admission was relapse investigation and treatment (51.6%), followed by rituximab infusion (18.6%) and diagnostic workup (16.3%).

The overall relapse rate was 0.79/year in RRMS patients, and 0.10/year for SPMS. Majority of the relapses occurred while off a DMT (72.7%). The relapse rate after DMT commencement was significantly lower than the relapse rate before DMT (0.59 vs 0.90 relapses/year, p = 0.042) (Table 1).

Two patients underwent plasma exchange as relapse treatment, while the rest of the patients received IVMP for relapses.

Disease modifying therapies

The mean duration between MS diagnosis and to starting DMT was 22.2 months (SD = 37.9) for RRMS patients and 69.8 months (SD = 79.9) for SPMS patients in the cohort. Most of the patients (82.65%; 81/99) had not received DMT prior to their first visit to AKUHN, of which 81.5% (n = 66/81) were RRMS patients (Table 2). Of the patients who had received DMT prior to their first visit in AKUHN (n = 17/99), 5 patients had SPMS. About 32 patients (48.5%) with RRMS had DMTs initiated for the first time when they visited

AKUHN. Approximately 48% of patients (n = 47/99) never received DMT at all, of which 34 had RRMS. Visiting AKUHN was significantly associated with DMT initiation (p < 0.001) (Table 2).

Sixteen patients experienced challenges in maintaining adherence to DMTs, intolerance (11 patients), and financial toxicity of DMTs (5 patients) being the most common reasons. Eleven patients were noncompliant to DMT, commonly due to financial constraints.

The most commonly prescribed DMT was interferon beta 1 A (55.7%), followed by glatiramer acetate (15.38%) (Figure 3).

Missing data

The variables with large amounts of missing data included results of relevant investigations done prior to visiting AKUHN, such as MRI and CSF results, and EDSS values were not evaluated in any of the patients.

Discussion

This is the largest registry cohort to date from Kenya. MS presented predominantly with opticospinal disease at onset. RRMS was the most common type of MS. Neuroimaging, and thereby, diagnosis was delayed by 5 years. Relapses were predominantly treated with IVMP. Patients with RRMS were

Table 2. DMT use in MS patients – Placed after section on disease modifying therapies.

|			
Patients who received DMT prior to Visit 1 (n = 98)			
	Relapsing MS	12	12.24%
	Progressive MS	5	5.10%
Patients on DMT on contact with AKUHN (n = 97)			
	Relapsing MS	6	6.19%
	Progressive MS	2	2.06%
Patients first DMT initiated at AKUHN (n = 98)		36	36.73%
	Relapsing MS	32	
	Progressive MS	4	
	PPMS	0	
	SPMS	4	
Patients DMT usage at last visit	On DMT	40	40.40%
	Not on DMT	59	59.60%
DMT initiation in RRMS patients	Ever	Never	Total
PREAKUHN	11	67	78
AKUHN	37	41	78
Total	48	108	156
Specific challenges with DMT (n = 20 from 16 patients)			
	Intolerance	11	55.00%
	Financial issues	5	25.00%
	Drug unavailability	2	10.00%
	Pregnancy	1	5.00%
	Others	1	5.00%
Reasons for non-compliance (n = 11)	Unknown	5	45.45%
	Cost/financial difficulty	2	18.18%
	Stress	1	9.09%
	Wants to change DMT	1	9.09%
	Parent not available to inject	1	9.09%
	Unavailability of smaller needles for injection	1	9.09%
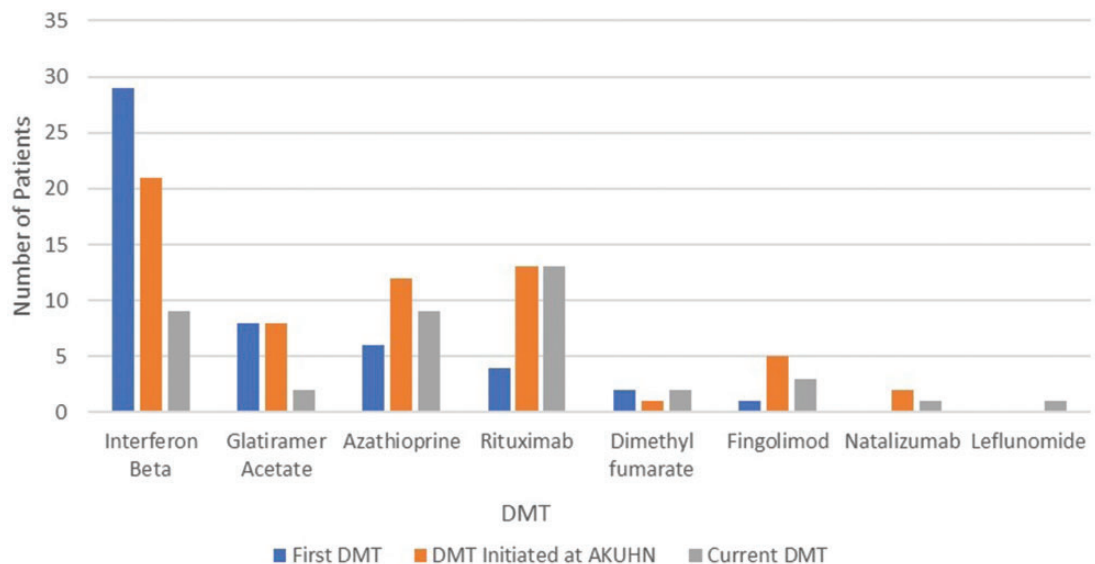
Figure 3. DMT used by patients with MS.

more likely to be initiated on DMT (mostly interferon beta 1a), after which there were notable issues with adherence.

Demographics and comorbidities

Our registry cohort is similar to others in SSA. The female to male ratio of 4:1 is comparable to the sex ratio of 7:2 found in a small study conducted in Nairobi,[6] although a higher female preponderance has been found in AA.[12,13] Most of our patients were indigenous black Africans. This is in contrast to previous studies in South Africa, whereby majority of the patients are white, with blacks constituting a minority.[14–16] The study in Sudan mainly involved patients of Arab-African ethnicity.[17]

The majority of our patients had comorbidities especially psychiatric – mainly depression – which is a known common comorbidity generally in MS.[18] Over half (54%) of our patients had vitamin D insufficiency/deficiency; although the MS Sunshine Study concluded Vitamin D was not associated with MS risk, duration of UV exposure was which may be relevant to our finding.[19]

Other common comorbidities in our cohort included dyslipidemia, thyroid disorders (goitre/hypothyroidism) and vitamin B12/folic acid deficiency. According to meta-analyses, the most prevalent comorbidities in PwMS were depression, anxiety, hypertension, hyperlipidemia and chronic lung disease.[18] Meningiomas, inflammatory bowel disease and irritable bowel syndrome, epilepsy, early cataracts and restless legs syndrome were also found to be more common than expected in the MS population. In contrast, only 2% and 3% of this cohort suffered from epilepsy and restless legs syndrome respectively. Only 4 of our patients had vitamin B12 deficiency. Although vitamin B12 deficiency leads to demyelination, the association with MS is somewhat unclear. Majority of patients with MS do not have detectable vitamin B12 deficiency.[20]

Only 9% of our patients had a history of tobacco smoking. In meta-analyses, smoking has a significant association with MS risk. Possible mechanisms for this include increased blood-brain barrier permeability, cyanide-related CNS demyelination and nitric oxide-related axonal degeneration and conduction block.[21]

Two of our patients had a history of unilateral/bilateral hip avascular necrosis (AVN). However, the aetiology of AVN was not clearly documented in the patient charts. Both patients had 5–6 relapses. It is most likely that these could be steroid-related. There have been a number of case reports and case series describing AVN in PwMS.[22]

Clinical and diagnostic characteristics

The mean age of onset of symptoms was 30.7 years with a delay of 4 years to diagnosis. This is comparable to e.g. Nigeria,[23] but the delay-to-diagnosis is twice as long when compared to e.g. a 2006 study in North America which revealed a delay of 2.2 years.[12] Approximately 80% of our patients had RRMS which is more than the globally reported mean.[24] Most of our patients had weakness, sensory symptoms or optic neuritis which is similar to the other study from Kenya[6] and Nigeria.[23]

Only five percent of our patients had a positive family history of MS. Familial aggregation of PwMS has commonly been described in areas of high prevalence, such as Europe,[25–27] as well is in the Middle East and North Africa (MENA) region[28] which is thought to be due to a higher consanguineous marriage rate. Globally, the prevalence of familial MS is estimated at 12.6%.[29]

The delay from symptom onset to first MRI was 5.04 years, and 53% of patients had their first MRI at another facility prior to visiting AKUHN. This reflects the relative lack of availability of MRI diagnostic services in our region, compounded by probably missed diagnoses due to a severe scarcity of neurologists. There are only 18 neurologists in Kenya for a population of 50 million and most are based in the capital. In the other study from Nairobi, 5 of the 9 patients had travelled abroad specifically for MRI scanning,[6] reflecting that there has indeed been a rise of MRI diagnostics over the last two decades but there is still a large gap in service.

Most patients (76%) had not had CSF studies done prior to their first visit to AKUHN. In Sudan, only selected patients underwent CSF OCB and VEP testing due to decreased access to such diagnostics.[17] After visiting our institution, and additional 39% underwent CSF analysis, with our laboratory being one of the few in the region that offer OCB testing.

DMT role, compliance and challenges

The time to first relapse was significantly shorter in the RRMS group than the SPMS group. Patients were more likely to receive DMT at our facility as compared to another facility, probably due to our hospital having the highest concentration of

neurologists compared to any other centre in the capital. The mean duration from MS diagnosis to initiation of DMT was 22.2 months; interestingly some patients were started on DMT even before the diagnosis was confirmed as reflected in SD. Data from the Big MS Data Network suggests that DMT should be initiated within 6 months from disease onset in order to prevent long-term disability.[30] Two important effects from visiting our institution were noted: the increased DMT prescribing translated to few documented relapses in the RRMS group, and patients on DMTs were more likely to stay on them at last follow-up.

Interestingly, 4 patients with SPMS had DMTs initiated too, which is less than those SPMS patients on DMTs before they came to our hospital (reflecting the non-specialist care they could have been receiving). On personal review of these cases with the neurologists concerned, it seemed the main reason was that these cases were under the ambiguous "relapsing-progressive" category, one which does not help on DMT decision making. However, the category relapsing-progressive MS has been eliminated and is no longer used.[10]

More than half, 34 of 47 patients (53%) who had never received DMT had RRMS. Comparatively, in a study in Nigeria, 3 out of 5 patients were on DMT (60%),[23] and none of the Sudanese cohort received DMT as the agents were not locally available.[17] DMT availability is much higher (mean of 77%) in high-income countries as well is in the MENA region.[6]

DMTs are available in Kenya for PwMS. However, data on accessibility to DMT in Kenya is lacking, especially in the government healthcare facilities. Despite the availability of DMT in our institution (private), 21% of our patients were noncompliant, most commonly due to financial constraints. Studies looking at adherence to IFNB and glatiramer acetate, indicate that 60–70% of patients adhere to treatment for 2–5 years,[31] and the usual reason for not continuing was due to the discomfort or reluctance of self-injecting. The costs of DMT for MS in the United States have been shown to be high and rising with time. This has been a major concern among health care providers and patients.[28]

The most commonly initiated DMT in AKUHN was IFNB (33.8%), followed by rituximab (20.97%). We have looked at our registry since the completion of this study and rituximab is now the most commonly prescribed DMT at our institution. This is because it is readily available at our institution and is the most cost-effective and convenient DMT for patients.

Limitations of this study include the generalizability of results and missing data. The study was conducted in a private tertiary health facility whereby patients of different nationalities are seen, unlike that in most public healthcare facilities in Kenya. This study probably therefore, would not be representative of the state of MS in the country as a whole. Given the retrospective nature of this study, missing data was also a challenge, especially for laboratory results that were done prior to the availability of an electronic data system in our institution. In addition, there were no EDSS scores on any of the medical records that were reviewed.

Conclusion

MS in Kenya is not rare and the overall phenotype is similar to other countries in Africa and blacks in North America. The majority of our cohort has RRMS. There was no difference in disability between native black Africans and other races at their first visit to AKUHN. There was a significant delay between symptom onset and neuroimaging, which leads to a delay in diagnosis and treatment. There was also a prolonged duration between diagnosis and initiation of DMT. Relapse rates were reduced after introduction of DMT. Relapses were mainly treated with IVMP.

This study demonstrates similarities between MS patients at AKUHN and AA PwMS in North America, and also highlights key challenges regarding DMT availability and compliance in our patients. Given that our patient population was heterogeneous, it is important to have more studies conducted in government health facilities, in order for us to have a better understanding of MS in the Kenyan population. In addition, creation of a national MS registry would enable us to have a database of patients, for further research and for more comprehensive care, and encourage government agencies to participate in making DMT more widely accessible.

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Supplemental Material

Supplemental material for this article is available online.

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