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Clinical Presentation Of Multiple Sclerosis In A Tertiary Health Care Centre, Abuja

Gerald Awele Onwuegbuzie*, Peter Alabi
Neurology Unit, Department of Medicine, University of Abuja Teaching Hospital, PMB 228,Garki Abuja, Nigeria ZIP-900243

ABSTRACT

Multiple sclerosis is one of the most important immune mediated inflammatory diseases which affect young adults in their productive years and contributes to disability and mortality. Multiple sclerosis (MS) is an immune-mediated inflammatory disease of unknown definite aetiology which result from abnormal activity of the body's immune system characterized by attacks of the myelinated axons in the central nervous system. The aim of this study is to demonstrate the clinic presentation of multiple sclerosis among Nigerian patients. The study which is a descriptive cross-sectional study was carried out at a tertiary health centre, from January 2011 and December 2020. A total of thirty-six patient had structured questionnaire administered in the Neurology Clinic and patients admitted into the medical wards. However, twenty-four patients were analyzed. The mean age of onset was 31.8 ± 8.8 with a female preponderance (91.7%). The clinical presentation of patients with multiple sclerosis showed that 95.8% had limb weakness and 87.5% had limb paraesthesia. Limb ataxia and fatigue was seen in 79.2% and 75% of the patients respectively, while 66.7% had limb spasticity and 54.4% had incoordination. The Clinical course of the disease showed that relapsing-remitting disease was seen in about 79.2% and secondary progressive is about 16.7%. This study though hospital based, suggest that MS is not uncommon among Nigerian. The 10-year period needed to get the study number may be a result of most patients being lost at the secondary health facilities due to non-recognition of the early symptoms and signs and poor diagnostics facilities.

Keywords: Multiple sclerosis, Clinical presentation, Nigeria.

*Corresponding Author Email: gerawele@yahoo.com
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INTRODUCTION

Multiple sclerosis is one of the most important immune mediated inflammatory diseases which affect young adults in their productive years and contributes to disability and mortality. Multiple sclerosis (MS) is an immune-mediated inflammatory disease of definite unknown aetiology which result from abnormal activity of the body's immune system characterized by attacks of the myelinated axons in the central nervous system. It is thought that MS affects approximately 2.1 million people Worldwide [1]. Attempts have been made to unravel the cause of MS but this has remained elusive though the prevalence tends to increase with latitude. In the geoepidemiology of MS there is a clear latitudinal variation with respect to the frequency. It has been demonstrated that higher latitude may lead to increase in the incidence and prevalence as well as a more severe outcome. In some studies gradients have been demonstrated between prevalence and latitude, [2,3,4,5,6] where as in other studies no association was found.[7,8] A meta-analysis by Samson et al demonstrated a statistically significant positive association between MS prevalence and latitude globally.[9]

MS has remained complex disorder, in which environmental agents play a role in a genetically susceptible individuals, with a subsequent trigger of an auto-aggressive immune attack on the myelin sheath and other components of central nervous system (CNS) axons. [10] However, the sequence of events that initiates the disease remains largely unknown.

The pathogenesis comprises of an inflammatory process in which there is a cellular and humoral immune response to central nervous system antigens and neurodegenerative process involving neuronal loss and subsequent brain atrophy [11-13]

Demyelination and remyelination often occurs in multiple sclerosis, although remyelination require generation of new oligodendrocytes[14] most chronic lesions are not remyelinated. Studies have shown that remyelination occurs in early disease stage seen at biopsy and postmortem examination.[15-18]

Accurate clinical diagnosis has remained elusive in developing countries leading to delayed diagnosis and management. The Macdonald criteria provided a fairly sensitive method which can be used for the diagnosis.[19]

MS is often recognizable clinically not as a unified disease entity hence the symptoms are extremely varied and depend on the location of the lesion as well as the severity of the attack. This has made diagnosis more difficulty more in the developing countries leading to incorrect/delayed diagnosis of MS with considerable consequences for patient management.[20,21.]

Multiple sclerosis (MS) is diagnosed based on presence of inflammatory and demyelinating injury with objective involvement of the central nervous system (CNS) that is disseminated in

both time and space as well as no better explanation for other diseses.[22,23] Diagnosis is therefore based on the clinical features, magnetic resonance imaging (MRI) and the exclusion of other diseases that have similar presentation.

Dissemination in time refers to two or more episode of evidence of inflammatory disease activity not less than one month apart,[19,24] while disseminated in space refers to magnetic resonance image (MRI) evidence of disease process in not less than two discrete central nervous system neuroanatomic area. Thus, the clinical features vary considerably between patients and even the episodes and also depend upon the site of neurologic lesion. In a majority of cases patients will present with a wide variety of symptoms such as sensory and motor involvement, impaired vision, difficulty with balance and coordination, and gait impairment. The aim of this study is to demonstrate the clinic presentation of multiple sclerosis among Nigerian patients.

MATERIALS AND METHOD

Study location and Data collection

The study was carried out at the University of Abuja Teaching Hospital, a tertiary health centre, from January 2011 to December 2020. It is a descriptive cross-sectional study. A total of thirty-six patient had structured questionnaire administered to them in the Neurology Clinic and patients admitted into the medical wards. However, twenty-four patients were analyzed, with eight having alternate diagnosis and the rest having incomplete investigations.

The diagnosis was based on patient full clinical assessment clinical, magnetic resonance imaging (MRI)of brain and spine, Cerebrospinal fluid oligoclonal band.

Brain MRI was done using a 1.5 Tesla machine were axial and sagittal views of T1- and T2-weighted images (WI), fluid-attenuated inversion recovery (FLAIR) images, and in some cases spine MRI.

The final diagnosis of Multiple sclerosis was done based on 2010 McDonald criteria. [i) Two or more clinical attacks with objective clinical evidence of 2 or more lesions. ii) Two or more attack with objective clinical evidence of 1 lesion and dissemination in space demonstrated greater than one T2 lesion on MRI. iii) One attack with objective clinical evidence of greater than two lesion by MRI. iv) One attack with objective clinical evidence of one lesion by MRI-Clinically isolated syndrome. v) Insidious neurologic progression suggestive of multiple sclerosis (Primary progressive multiple sclerosis)]. The 2017 McDonald criteria was not use since the study commenced in 2011.

Other investigations to exclude Multiple Sclerosis mimicker were done including Vitamin B12, Erythrocyte sedimentation rate, Antinuclear antibodies, Anti- dsDNA, Glycated

Hemoglobin, Rheumatoid Factor, HIV screening and Aquaporin-4 antibodies. (Anti-AQP4 antibodies were determined in the serum of the patients)

The questionnaire presented had questions about: (1) demographic aspects (gender, age, income and educational level) (2) Symptom Profile (3) Brain and Spine MRI findings, and other laboratory investigation finding. (4) Clinical course and present medication.

Inclusion Criteria

All patients who were admitted into the medical ward with confirmed Multiple Sclerosis. All patients had full clinical assessment for Multiple Sclerosis and screened by McDonald criteria from January 2011 to December 2020 were included in the study.

Exclusion Criteria

Patients who had space occupying lesion with neurological deficits or metastatic brain disease and those with Human Immunodeficiency Virus with neurological deficits were excluded from this study. Also excluded from the study were those who were unconscious and those who had motor and/or expressive aphasia, other idiopathic inflammatory Demyelinating disorders, Idiopathic or post infective transverse myelitis were not included. Those patients with anti-AQP4 antibody positive, MRI brain negative and cerebrospinal fluid oligoclonal bands that were negative. Patients with single episode or recurrent longitudinally extensive transverse myelitis with cord lengths of more than 3 vertebral segments were excluded.

Data analysis

Statistical analysis of data collected was performed using Analyse-it v4.5 statistical software for Microsoft Excel. Data collected was analyzed by frequency, mean, standard deviation and chi-square test. For all statistical tests, the threshold of significance is fixed at 5%. P-value>0.05 indicates none significant results. P-value<0.05 indicates significant results.

RESULTS AND DISCUSSION

A total of thirty-six patient had structured questionnaire administered in the Neurology Clinic and patient admitted into the medical wards. However, twenty-four patients were analyzed, with eight having alternate diagnosis and the rest having indeterminate diagnosis due to incomplete investigations.

Table 1 Shows the baseline characteristics of the patients. Nineteen of them were less than 40 years of age with a female preponderance (91.7%). Most had tertiary education (82.6%) with 4(17.4%) being diagnosed during the pregnancy/postpartum period. The mean age of onset was 31.8 ± 8.8.

Table 1: Baseline Characteristics of patients diagnosed with Multiple Sclerosis

Characteristics	N	Mean ± SD
Age, years	**24**	34.6±**8.7**
		n (%)
Age, years		
<21	24	1(4.0)
21 – 30		7(29.2)
31 – 40		11(45.8)
41 – 50		4(16.7)
51 – 60		1(4.2)
> 60		0(0.0)
Gender		
Females	24	22(91.7)
Males		2(8.0)
Marital status		
Single	24	12(50.0)
Married		12(50.0)
Occupation		
Civil servant	24	5(20.8)
Private Sector		2(8.3)
Self-employed		6(25.0)
Student		3(12.5)
House-wife		4(16.7)
Unemployed		4(16.7)
Educational status		
Secondary	24	5(20.8)
Tertiary		19(79.2)
Family history of Hypertension	24	3(12.5)
Family history of Diabetes	24	0(0.0)
Pregnancy/Postpartum status		
Yes	**24**	4(16.7)
No		18(75.0)
Not applicable		2(8.3)
Pregnancy/Postpartum stage		
1st trimester	3	0(0.0)
2nd trimester		1(33.3)
3nd trimester		0(0.0)
1st 3 months postpartum		2(66.7)
Clinical Characteristics		**Mean ± SD**
Age at symptom onset, years	24	31.8 ± **8.8**
Age (years) at diagnosis, years	24	33.8 ± **8.9**
[a]Duration of illness, years	24	2.0(1.0-4.5)
[a]Number of exacerbations	24	2.0(2.0-4.0)

Table 2 shows the clinical presentation of patients with multiple sclerosis, of which 95.8% had limb weakness and 87.5% had limb paraesthesia. About 79.2% had limb ataxia, Fatigue was seen in 75% of the patients, 66.7% had limb spasticity and 54.4% had incoordination.

Table 2: Clinical Presentation of patients diagnosed with Multiple Sclerosis

	N	Present n (%)	Left n (%)	Right n (%)
Optic Neuritis	24	7 (29.2)	7(29.2)	7(29.2)
Acquired MCB	24	3(12.5)	2(8.3)	1(4.2)
Oscillospia	24	0(0.0)	0(0.0)	0(0.0)
Acquired binocular diplopia	24	2(8.3)	2(8.3)	2(8.3)
Unilateral facial palsy	24	3(12.5)	2(8.3)	1(4.2)
Unilateral diminution of hearing	24	1(4.2)	0(0.0)	1(4.2)
Transient acute NP vertigo (under age 40)	24	3(12.5)	3(12.5)	3(12.5)
Internuclear opthamoplegia	24	0(0.0)	0(0.0)	0(0.0)
Ophthalmoplegia	24	1(4.2)	0(0.0)	1(4.2)
Facial spasm	24	1(4.2)	1(4.2)	1(4.2)
Trigeminal Neuralgia	24	1(4.2)	1(4.2)	0(0.0)
Other facial paraesthesia	24	4(16.7)	2(8.3)	4(16.7)
Limb ataxia	24	19(79.2)	19(79.2)	19(79.2)
Tremor	24	10(41.7)	10(41.7)	10(41.7)
Incoordination	24	13(54.2)	13(54.2)	13(54.2)
Dysarthria	24	7(29.2)	7(29.2)	7(29.2)
Dysphagia	24	2(8.3)	2(8.3)	2(8.3)
Limb Weakness	24	23(95.8)	15(62.5)	8(33.3)
Limb Spasticity	24	16(66.7)	16(66.7)	16(66.7)
Limb Paraesthesia	24	21(87.5)	21(87.5)	21(87.5)
Bowel dysfunction	24	4(16.7)	NA	NA
Bladder dysfunction	24	6(25)	NA	NA
Sexual dysfunction	24	3(12.5)	NA	NA
Impaired mobility	24	12(50)	NA	NA
Lhermitte's	24	1(4.2)	NA	NA
Uhthoffs	24	8(33.3)	NA	NA
Useless Hand of Opperheims	24	4(16.7)	NA	NA
Peduncular hallucinosis	24	1(4.2)	NA	NA
Pulfrich phenomenon	24	1(4.2)	NA	NA
Transient paroxysmal Neurologic events	24	6(25)	NA	NA
Fatigue	24	18(75.0)	NA	NA
Seizures	24	2(8.3)	NA	NA
Cognitive Impairment	24	1(4.2)	NA	NA
Depression	24	8(33.3)	NA	NA

Figures 1 shows the Clinical course of the disease. The relapsing-remitting disease showed about 79.2% and secondary progressive is about 16.7%.

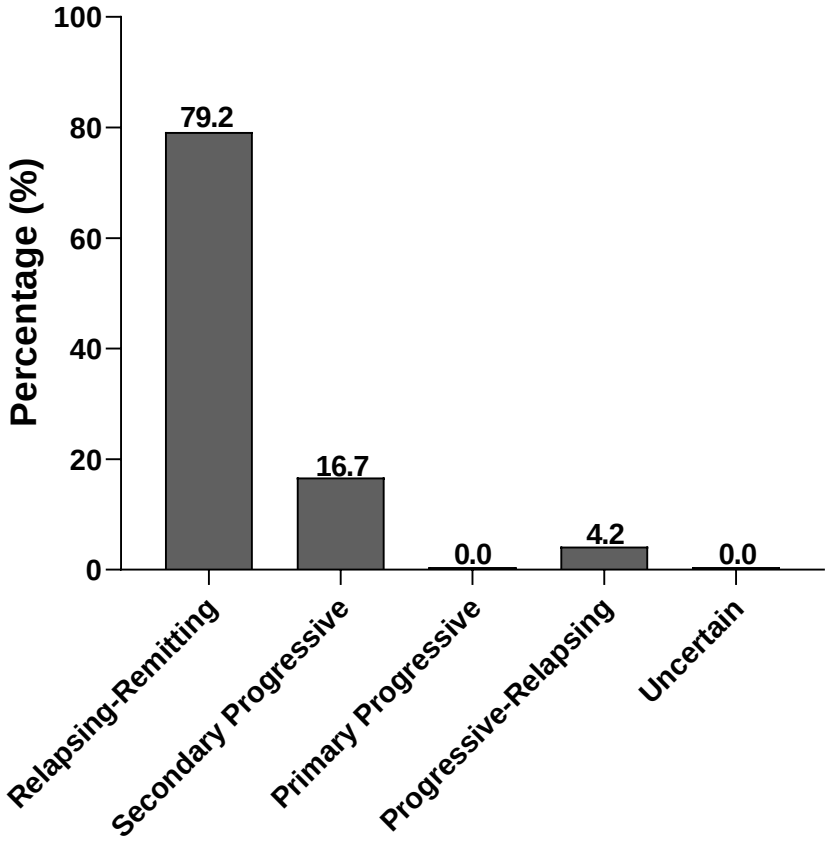

Figure 1: Clinical Course of Disease

Table 3 Showed that 75% had lesions in the periventricular area, while 45.8% of lesions were seen in both the Juxtacortical and cerebellum.

Table 3: MRI findings in patients diagnosed with Multiple Sclerosis

(Patients with MRI results, N = 24) Parts of the brain	Abnormality Present n (%)	Side of the body affected		
		Left n (%)	Right n (%)	Bilateral n (%)
Periventricular	18(75)	16(66.7)	17(70.8)	1(4.2)
Juxtacortical	11(45.8)	10(41.2)	9(37.5)	0(0.0)
Basal ganglia	4(16.7)	3(12.5)	4(16.7)	0(0.0)
Thalamus	1(4.2)	1(4.2)	1(4.2)	0(0.0)
Callosal and Peri-callosal	3(12.5)	1(4.2)	1(4.2)	1(4.2)
Dawson's Finger	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Brainstem	-	-	-	-
Midbrain	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pons	2(8.3)	0(0.0)	0(0.0)	0(0.0)
Medulla	1(4.2)	0(0.0)	0(0.0)	0(0.0)
Cerebellum	11(45.8)	6(25)	11(45.8)	0(0.0)
Cervical Cord	1(4.2)	0(0.0)	0(0.0)	0(0.0)
Thoracic Cord	4(16.7)	0(0.0)	0(0.0)	0(0.0)
Lumbosacral	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Lumber Cord	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Sacral Cord	0(0.0)	0(0.0)	0(0.0)	0(0.0)

Table 4 shows that 95.8% of the patients had methylprednisolone for treatment of acute relapse, while 4.2% had plasmapheresis. Interferon was used in 20.8% of patient, while 16.7% were on Dimethyl fumarate and one patient is on Cladribine (4.2%). There are 62.5% of the patients on Vitamin D and 41.7% were on Baclofen

Table 4: Medication used for Patients with Multiple Sclerosis

	N	n(%)
ACUTE RELAPSE TREATMENT		
Methylprednisolone	24	23(95.8)
Plasmapharesis	24	1 (4.2)
DISEASE MODIFYING THERAPY		
Dimethyl fumarate	24	4(16.7)
Interferon -beta 1a	24	5 (20.8)
Azathioprine	24	3 (12.5)
Cladribine	24	1(4.2)
THER MEDICATIONS		
Vitamin D	24	15(62.5)
Baclofen	24	10 (41.7)
Gabapentin	24	5 (20.8)
Selective serotonin reuptake inhibitors	24	2 (8.3)
Oxybutinin	24	1 (4.17)

DISCUSSION

In our study, 79% of the patients were less than 40 years of age with a mean age of 34 years. This is similar to previous studies which have shown that the commonest age group affected remains the young. [25-29] In Africa, a study in Sudan had 72.3% of their patients less than 40 years of age with a mean age of 35 years.[30] In previous studies the male to female ratio in patient with multiple sclerosis has found to vary depending on the region.[31] In our study we found a female preponderance of 92% with a female to male ratio of 11:1. The findings of female preponderance is similar to those found in most autoimmune disease, though ours is higher than some of the studies previously done. Ibrahim et al in Sudan found 83.3% female preponderance, with a female to male ratio of 5:1 in MS.[30] This is lower than the result of Yaqub et al in Saudi Arabia which showed female to male ratio of 1.4:1,[32]as well as studies done in Kuwait and Jordan[33-35] and northern Japan where the female to male ratio is 3.38: 1. [36] Overall, however there remains a female preponderance in most studies though with varying proportion.

The study showed clinical presentation with a diverse range of symptoms which has been noted by previous authors. [37,38] The commonest clinical presentation of patients with multiple sclerosis in our study group was limb weakness in 95.8% and limb paraesthesia in 87.5%. This is similar to the study by Inshasi et al in Dubai with a prevalence of motor symptoms in 72.78%, followed by sensory (48.41%) [39] and El Salem et al in Jordan with the most common symptom as motor at 30.8%.[40] The Saudi Arabia study by Daif et al also had a similar pattern

of 61.8% motor and 54.2% sensory symptoms.[41] In Africa, Abu-Elbishir et al in Sudan had 85% of motor and 85% of sensory symptoms.[42] Overall there is dominance of motor and sensory symptoms in most previous studies, however the relatively higher frequency of motor and sensory symptoms at the time of presentation could be related to lack of awareness of the disease, difficulty with diagnoses of MS, delay in diagnostic imaging due to limited availability, and limited availability of proper neurological review.

Our study also had 75% of the patient complaining of fatigue. This is similar to the report by Minden et al who found fatigue in about 83% of patient studied. Ocular symptoms were seen only in 29% of patient this lower than previous studies done. Ocular manifestation in MS vary remarkably, the study by Ibrahim et al in Sudan had 60% of ocular manifestation,[6] and Najim Al-Din et al found a prevalence of 28.6%.[43] However Inshashi et al in Dubai found a prevalence of 16.13% which is lower than those found in the study.[39]

Spasticity affects quality of life in MS patient especially when painful. In our study limb spasticity was seen in 66.7%. Cerebellar presentation in our study was characterized by limb ataxia, incoordination, tremor and dysarthria representing 72.9%, 54.4%, 41.7% and 29.2 % respectively. Ibrahim et al in sudan, Africa found lower values for cerebellar sign 4.6%,18.4% 10.7% and7.6% respectively.[30] The study by Inshashi et al in Dubai had cerebellar presentation of 19.98%. The reason for our higher values may be related to late presentation of most of our patients.

Seizure was found in 2(8.3%) of the patients in our study. Low level was also recorded in other studies which recorded 5 cases.[41] Overall the incidence of seizure is low, occurring in 2-3% of patients with Multiple Sclerosis.[44]

In terms of the clinical course of the disease, our study shows that relapsing-remitting disease occurred in about 79.2% and secondary progressive is about 16.7% and progressive-relapsing was 4.2%. This is consistent with previous studies done with relapsing remitting 72.4%, secondary progressive 11.7% and progressive relapsing 6.0%.[39]

Neuroimaging has improved our ability to make a diagnosis in multiple sclerosis patient and assessing the extent of the lesion and excluding other possibilities. The MRI finding in our study showed that 75% of the lesion were in the periventricular area and 45.8% of the patient had lesions in both the Juxtacortical and cerebellum. Neuroimaging has gained so much importance, such that appropriate MRI abnormalities has been integrated into the diagnostic criteria and presence of brain MRI T2-weighted lesion may suggest clinically definite Multiple sclerosis.[45] It is thought that T2-weighted MRI may reflect an ongoing process of inflammation, demyelination, gliosis as well as axonal loss.

For the medication use, our study found 95.8% used Methylprednisolone and 4.4% had plasmapheresis. Steroids are typically used in acute relapse due to their anti-inflammatory

effects, therefore accelerating recovery. With regards to the disease modifying drugs, a limited number of patients used the medication due to high cost and poor accessibility. Disease modifying therapies have been found to prevent/reduce clinical exacerbations and possibly delay the onset of disability. The main disease modifying drug used were Interferon-beta 1a 20.8%, Dimethyl fumarate 16.7% and Cladribine 4.2% and Azathioprine 12.5%. The use of steroid was higher in our study group as most of the patient were diagnosed during flare when compared to the Sudanese study which showed that only 65% of patient had Methylprednisolone, while 13% had Interferon Beta and 16% had Azathioprine.[42]

CONCLUSION

This study though hospital based, may suggest that MS is not uncommon among Nigerian as this data was for a 10-year period. The basis for this may be that the disease is truly rare among Nigerians or may be indication of poor diagnostic facilities. Subsequent community-based studies in Nigeria will be needed to determine the true prevalence rate. The motor and sensory presentation still remains the dominant in our study with a female preponderance.

CONFLICT OF INTEREST

The authors report no conflict of interest. The authors alone are responsible for the content and writing of this paper.

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