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Neuromyelitis Optica Spectrum Disorders in Africa (A Narrative Review of 622 Cases)

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Abstract

Neuromyelitis Optica spectrum disorders (NMOSD) are a group of inflammatory disorders of the CNS, characterized by severe attacks of optic neuritis and myelitis. There are very few epidemiological studies of NMOSD in Africa. The purpose is to provide descriptive details of all cases published and reported in scientific meetings, analyze epidemiological, clinical, paraclinical, therapeutic, and outcome profiles of NMOSD in Africa and compare our data with literature. Authors did a literature search using MEDLINE, EMBASE, SCIENCE DIRECT, and GOOGLE SCHOOLAR. The search further extended to international and local journals, as well as regional and national meetings for all reports and articles about NMOSD in Africa. Till the end of 2019, 622

cases were reported in Africa, originating from 21 countries. The average age at disease onset was 32.5 years and the women to men ratio was 2.78:1. The big majority of patients underwent both brain MRI and serum aquarporin-4 antibody testing. The prognosis was generally unfavorable, with motor and/or visual sequelae. This 1st report of NMOSD in Africa does not reflect reality; theoretical number is around 50,000 cases, due certainly to considerable gap with many under-diagnosed and certainly misdiagnosed cases, due to many factors.

Subject Areas

Neurology

Keywords

Neuromyelitis Optica Spectrum Disorders, CNS, Aquarporin-4, Antibodies, Africa

1. Introduction

NMOSD or Devic's disease, is a group of inflammatory disorders of the central nervous system, characterized by severe attacks predominantly affecting the optic nerves and spinal cord [1]. Once considered a subtype of multiple sclerosis (MS) [2], recent clinical, epidemiological, and immunological data indicate that NMO is a distinct clinical entity [3]. NMO can be distinguished from MS by the presence of a pathological serum autoantibody to aquaporin-4 (AQP4-IgG) [4] [5], in around 70% of cases, by the occurrence of severe optic and spinal attacks [6], and the severe disruption of blood-brain barrier [7].

In Africa, no population-based study was performed in NMOSD, only hospital-based studies, and very few reports were found.

Due to the scarcity of data in Africa about NMOSD, there is a need to collect available data across the African continent on this group of disorders.

The objectives of this review are:

- Enumerate all published papers or abstracts on NMO in Africa.
- Provide descriptive details of the phenotypes and impact of the disease especially in Africa.
- Compare data from different parts of Africa.

2. Patients and Methods

The authors performed a literature search using MEDLINE, EMBASE, SCIENCE DIRECT, and Google Scholar, and also searched in international and local journals to identify articles that examined the NMOSD in Africa. Combinations of keywords, such as "neuromyelitis optica", "Devic's disease" and matching it with "Africa", or with African countries, one by one. Terms entered as medical subject headings (MeSH) and text words. The reference list of the retrieved articles

also reviewed to identify publications on the same topic. The report included epidemiological studies, case reports either published as articles or reported in congresses.

Due to the different time of data collection, the authors used both 2006 and 2015 diagnostic criteria.

3. Results

From December 2000 till 31st December 2019, 622 cases of NMOSD in Africa. Cases originated from 21 countries: 138 from Morocco [8]-[14], 118 from Algeria [15] [16], 95 from Nigeria [17], 118 from Egypt [18] [19], 29 from South Africa [20], 16 from Senegal [21], and 14 from Tunisia [22] [23], and the remaining from 14 other African countries [21] [24] [25] (**Table 1**).

Data and the characteristics of each NMO cohort according to the region in each country represented in **Table 1**.

Table 1. Distribution of reported NMOSD cases in African by country.

Number	Country	Reported cases
1.	Morocco	138
2.	Algeria	118
3.	Egypt	118
4.	Nigeria	95
5.	Sudan	31
6.	South Africa	29
7.	Libya	27
8.	Senegal	16
9.	Tunisia	14
10.	Cameroon	12
11.	Chad	5
12.	Niger	4
13.	Mali	4
14.	Togo	3
15.	Ethiopia	2
16.	Burkina Faso	1
17.	Ghana	1
18.	Madagascar	1
19.	R.D. Congo	1
20.	Ivory Coast	1
21.	Uganda	1
Total cases		622 cases

The ratio of women to men was 2.79:1. The average age onset was 32.5 years (Figure 1).

These findings suggest a high number of under-diagnosed or misdiagnosed cases (Figure 2).

In Morocco, data were available regarding the number of cases reported from different regions. The data originated from the leading university hospitals of Casablanca, Marrakech, Fes, and Oujda. No data were available from Rabat. In terms of cases, Casablanca is the leading center with 64 cases, followed by Marrakech (Figure 3).

Within the most extensive published cohort from a tertiary hospital in Marrakech, the number of cases identified has been increasing over the past 15 years, coinciding with the increased recognition of the condition as well as with the first NMOSD African conference, held in Marrakech, on the fifth and sixth of February, 2016 (Figure 4).

Brain MRI and serum Aquaporin-4 antibody (AQP4-IgG) assay performed in all patients in Morocco. All patients treated by pulse methylprednisolone during the acute attack. Chronic immunosuppressive therapy used in 32 cases, plasma exchanges in 13 cases, and 42 received Rituximab.

Besides the 138 cases in Morocco, serum aquaporin-4 antibody testing performed for the 118 cases in Algeria, 14 in Tunisia, 12 out of the 16 cases in Senegal [21], and 3 out of 4 cases in Mali [25].

In most cases studied, the prognosis was generally unfavorable, with motor and/or visual sequelae.

In the Moroccan series, the authors noticed that the NMOSD associated with autoimmune diseases in 2.88% cases: 1.44% cases of systemic lupus erythematosus, 0.72% case with Sjogren's syndrome, 0.72% case with antiphospholipid syndrome, and one case with Hashimoto thyroiditis.

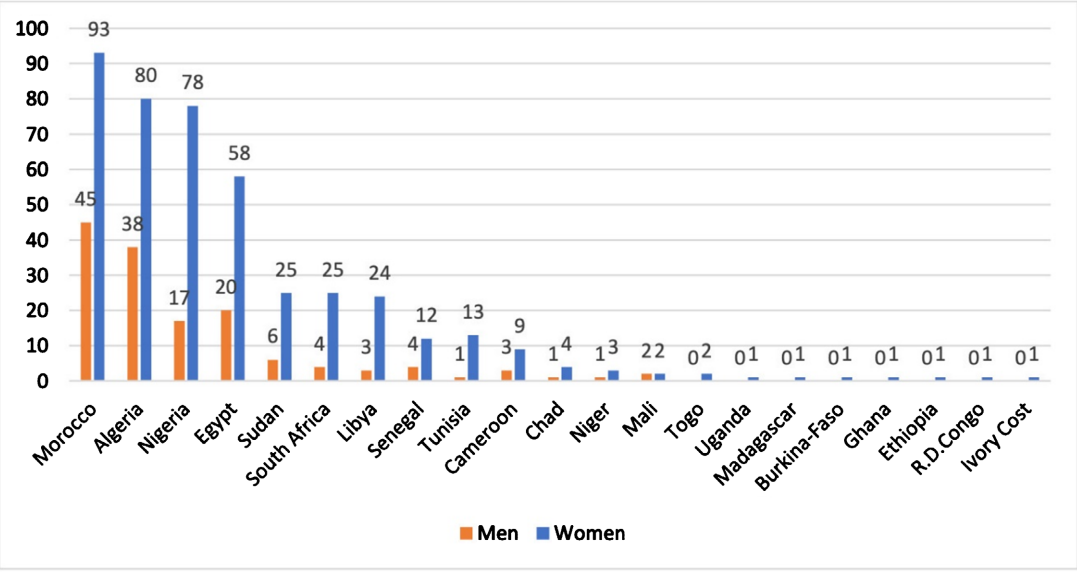

Figure 1. Distribution by gender of African NMOSD reported cases.

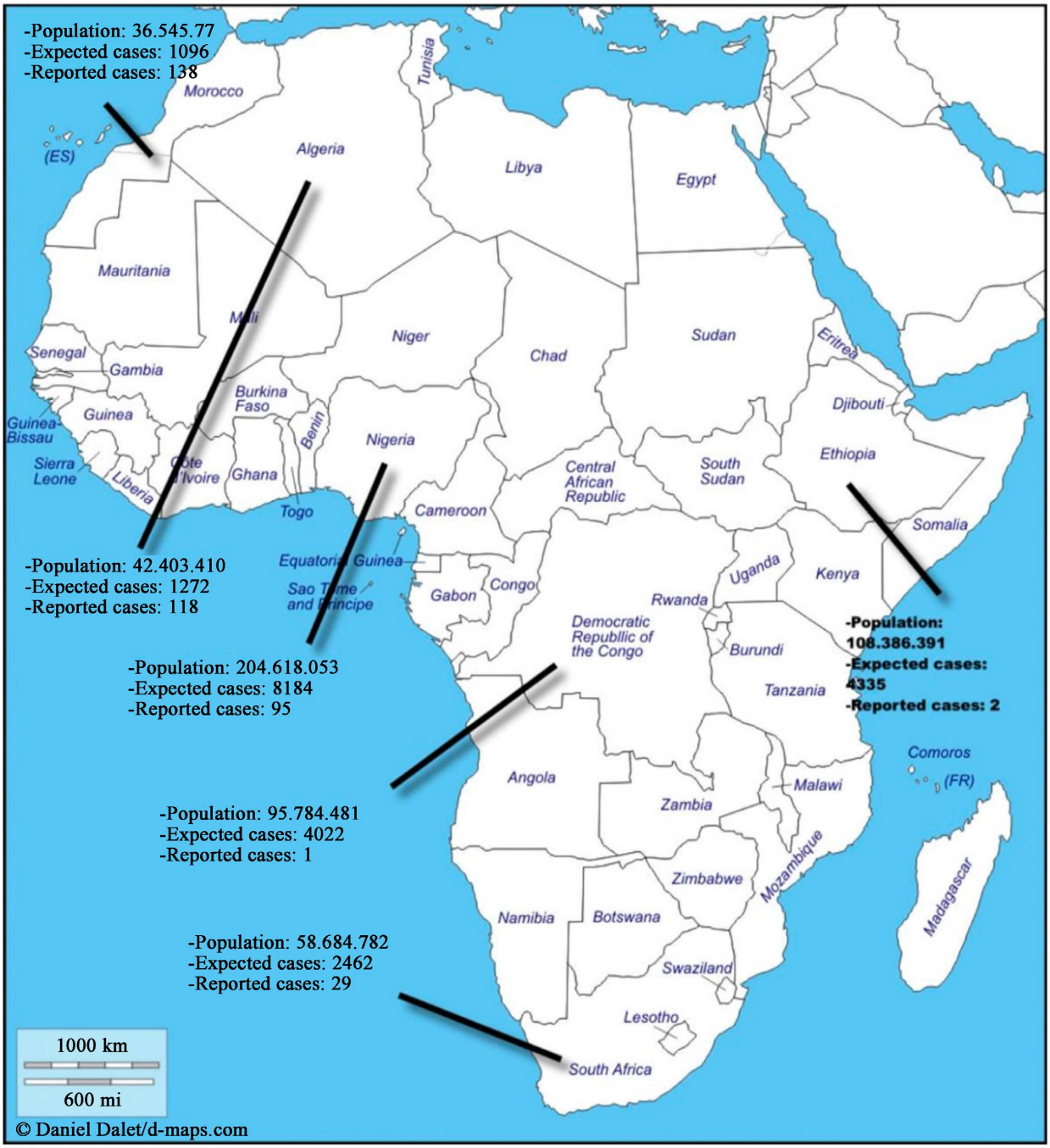

Figure 2. Map of Africa showing expected number of cases in more populated countries.

4. Discussion

This first review of all published and reported cases of NMOSD in Africa identified 622 cases [8]-[35]. Because of the high prevalence of this disease among the black ethnic groups of approximately 4.2/100,000, and assuming the population of Africa is 1.216 billion, with 75% being of black ethnicity, we would expect around 51,072 patients in whole of Africa [36]. These findings suggest a high number of under-diagnosed or misdiagnosed cases [36]. Theoretically, only

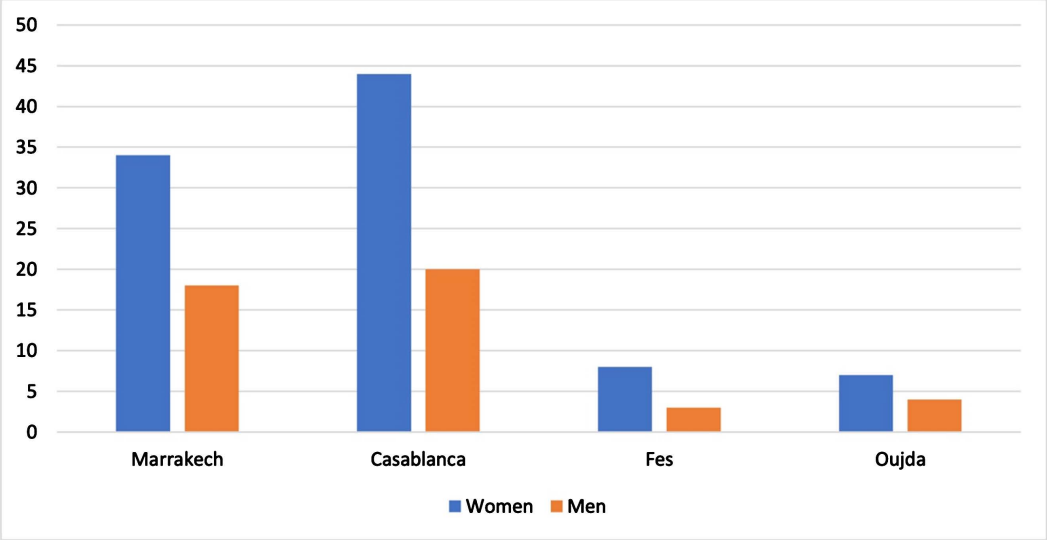

Figure 3. Distribution by age, gender, and region of the 138 Moroccan NMOSD reported cases.

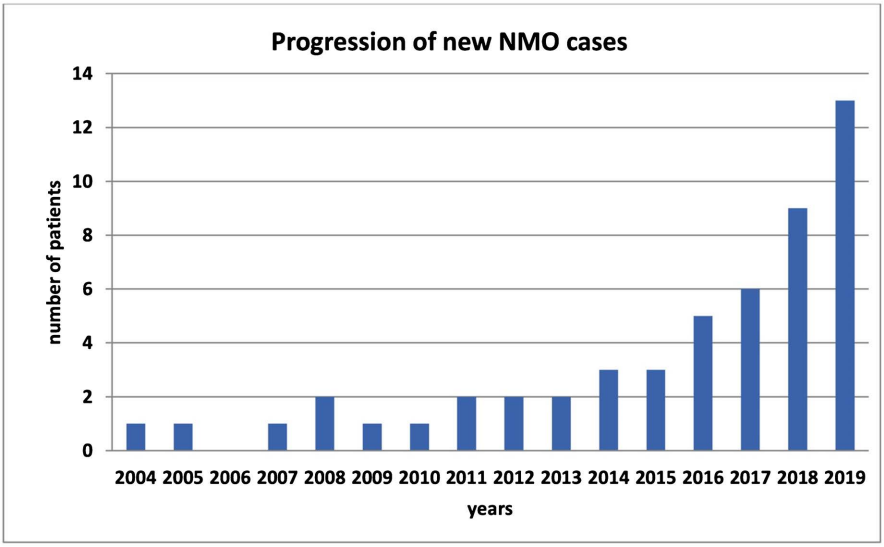

Figure 4. Reported NMOSD cases of Marrakech tertiary level hospital by year of admission.

1.21% of cases have reported. Limited resources, and lack of trained professionals are also, a likely to contribute to the underestimation of NMOSD in Africa. We can assume that this estimation could be much higher, if we took into account the population-based study in French Martinique that reported a higher prevalence: 11.5/100,000 in blacks (raising this estimation of NMOSD cases 139,000 cases) [37].

NMOSD is treated with long term immunosuppressive agents to reduce the risk of disabling relapses, and thus the consequent long-term disability and mortality. Incorrect treatment of NMOSD patients with MS drugs may worsen the condition. In addition, there is a common confusion of this condition with MS. Thus, a correct diagnosis of NMOSD is crucial to prevent mismanagement and harm.

The other surprising data is that 415 cases (66.7%) of reported cases were from North Africa, where black ethnicity is less important, while from the rest of the continent, with approaching 1 billion inhabitants, we collected only 207 cases (33.3% of all cases reported), indicating the considerable gap in Sub-Saharan Africa versus North Africa.

Since 2004, the first report of an antibody (NMO IgG) that distinguished NMO from MS was published [38]. A Canadian group did a systemic review to evaluate the worldwide incidence and prevalence of NMO, and highlighted the limited knowledge regarding the epidemiology of NMO and the importance of obtaining estimates standardized to general populations to enhance the comparability of studies from different countries [39].

Our study identified 622 cases reported from the whole of Africa, with the majority are from North Africa, may confirm the under-diagnosis and under-reporting in Sub-Saharan countries. Meanwhile, the black ethnicity, less dominant in north Africa, is the most concerned [40]. The cases mainly reported in Morocco (138 cases). This finding puts Morocco as a leading African country regarding the appropriate diagnosis of NMOSD. Analysis of the data showed that neurologists and sometimes others specialist, such as ophthalmologists and internal medicine specialist, are involved in the diagnosis and management of NMOSD cases.

Thus, the cases reported by neurologists alone may not reflects the total number of NMOSD patients in our setting.

In North Africa, the problem posed in terms of differential diagnosis is with MS. In Sub-Saharan Africa, where MS is very rare, infectious acute transverse myelitis constitute the main differential diagnosis. Especially in countries where access to AQP4-IgG assays remained limited and this could also contribute to under diagnosis.

AQP4-IgG seropositivity in NMO was 78% in Caucasian Germans [41] [42], 68% in a mixed American cohort [43], 62% in Danes [44], suggesting ethnic differences.

The pathophysiological mechanism underlying the association of NMO with other autoimmune pathologies, as pointed out in this series, is not fully understood: could it be a simple association of two autoimmune diseases in the same subject? Several authors have approved this hypothesis.

We suggest the following recommendations to address the diagnostic and management gap in Africa:

- Focus on education for better recognition of clinical and magnetic resonance imaging (MRI) features of NMOSD manifestations.
- Create non-governmental organizations (NGOs) and associations to fight against NMOSD by raising awareness and advocacy.
- Create specialized centers for the diagnosis of NMOSD.
- Implement magnetic resonance imaging (MRI) units and immunology laboratories for aquaporin-4 and MOG antibodies.

- Encourage North-South and especially South-South collaboration within Africa to share experiences.

5. Limitations of the Study

- Since there is no population-based NMOSD study performed in Africa so far, this report does not reflect the real prevalence or incidence of NMO-SD in Africa.
- The appropriate way of getting real data from Africa will require a registry where all African countries can report their cases, or for the conduct of well-designed population-based studies in several representative locations in Africa.

6. Conclusion

NMOSD is a heterogeneous group of disorders, it is marked in Africa by a considerable diagnosis and management gap, and the 622 cases reported do not reflect the reality. Indeed, thousands of cases are likely to be underdiagnosed or misdiagnosed with improper management and harm. Africa has a long way to go, in terms of education, sensitization, awareness, and collaboration to close the wide gap of NMOSD cases.

Conflicts of Interest

The authors declare no conflicts of interest.

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