Short communication

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ALS in Africa: current knowledge and exciting opportunities for future study – short communication

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Abstract

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease that can present with motor and extra-motor manifestations. Its global prevalence is 4.42 per 1 000 000, and it has a high mortality rate. In sub-Saharan Africa alone, 15 per 100 000 develop ALS mainly between their 40s and 60s and only one-fourth of them have access to treatment. ALS was found to be not only affected by genetic variation but also by the patient's mood and lifestyle. In Africa, males and younger people tend to be affected with ALS and rarely present with bulbar onset. ALS diagnosis is very challenging due to the lack of ALS-specific biomarkers and the sharing of some clinical features with other syndromes. ALS treatment is mainly riluzole and supportive treatment via nasogastric tube and ventilatory support. The access to treatment in Africa is very limited, thus a very bad prognosis with a median survival time of 14 months post-diagnosis. Further research is needed to assess the real situation in Africa and to try to closely monitor patients suffering from ALS.

Keywords: Africa, amyotrophic lateral sclerosis, neurodegeneration

Introduction

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder with variable motor and extra-motor manifestations with high mortality[1]. The global prevalence and incidence of ALS are ~4.42 per 100 000 population and 1.59 per 100 000 person-years, respectively[2]. The occurrence of ALS is higher in developed countries than in developing countries[2]. The clinical presentation of ALS is variable depending upon the involvement of different neurons[1]. Genetic variabilities can also affect the clinical profile of ALS patients[1]. Other risk factors include smoking, body mass index, physical work, head trauma, and chemical exposure[1]. The diagnosis can be made based on the El Escorial criteria[3], with simpler Gold Coast criteria proposed recently by Shefner *et al*.[4]. In addition to magnetic resonance imaging, nerve conduction studies and electromyography can help diagnose ALS[5]. The mainstay of ALS management is supportive treatment, which includes early ventilatory support and nasogastric tube feeding[1,5]. To date, riluzole is the mainstay of pharmacological therapy to improve survival time in ALS patients. Other drugs, such as edaravone and masitinib, are being investigated[5].

Though various studies have been done in developed countries, the studies done in the context of Africa are limited. In sub-Saharan Africa, the prevalence of ALS ranges from 5 to 15 per 100 000 population[6]. In Africa, the median age of onset ranged from 44.5 to 64.0 years, and only one-fourth of patients received riluzole[7]. The median survival time was 14 months from the time of diagnosis[7]. There were regional variations of the survival time within Africa, with maximum survival time in northern Africa and minimum in western Africa[7]. Another study revealed a higher mortality rate among South African ALS patients than in Portuguese, possibly due to less use of non-invasive ventilation and riluzole among African counterparts[8]. This difference in mortality between developing and developed countries warrants further investigation among ALS patients in the African continent.

Studies have found that the quality of life of ALS patients depends on mood disorders and non-motor symptoms[9]. Also, caregivers of ALS patients can be affected by negative emotional states and interaction of ALS patients with their family members. Hence, adequate interventions are needed to

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improve the quality of life of these patients[9]. These shreds of evidence highlight the need for further studies and a deeper understanding of ALS, its associated factors, and interventions needed to address various issues in patients and their caregivers. In this paper, we aim to understand the current situation of ALS in Africa.

Risk factors, clinical manifestations, diagnosis, and management of ALS in Africa

ALS among Africans has been associated with environmental and genetic factors (Fig. 1). Age, gender and family history of ALS, trauma, severe hypotonia in children, sensory changes, and spinal anesthesia have been considered as risk factors[10]. Lifestyle factors also include dietary habits, smoking, and drinking alcohol[11]. In Senegal, it was found that residing outside the city, being a farmer, and exposure to pesticides and chemical fertilizers are factors associated with ALS[11].

Environmental risk factors associated with ALS among the African population include exposure to diesel exhaust, lead, silica, organic dust, extremely low-frequency magnetic fields, electric shocks, and air pollution in the long term[12]. It has also been found that exposure to heavy metals, solvents, and manganese[13] are significant risk factors.

There is a genetic contribution to the development or occurrence of ALS among individuals. These genetic damages found in C9orf72, SOD1, TDP-43, and FUS genes are the risk factors for ALS[14]. These mutations are found in South Africa, where one individual had a likely disease-causing ANXA11 variant. Moreover, the TARDBP gene showed the highest mutation frequency among the cases in Tunisia[15].

Three ALS clinical manifestations are progressive muscle atrophy (PMA), progressive bulbar atrophy (PBA), and progressive bulbar palsy (PBP)[16]. In contrast to ALS patients in Western nations, males and younger people are more likely to have the disease in African patients, and bulbar onset is less common. Marin *et al.*[17] observed that among individuals of African descent, there are several distinct characteristics of ALS and that a lower incidence of ALS is observed among black individuals residing in Western countries, and individuals of African origin tend to experience a younger age of onset for the classic form of ALS.

Challenges for ALS diagnosis are due to the presence of various syndromes that imitate ALS. These syndromes share the same clinical features but are not related to ALS[18]. ALS is the most prevalent form among the four main classes of motor neuron diseases: ALS, primary lateral sclerosis (PLS), PMA, and PBP. A common symptom is progressive muscle weakness. The difficult diagnosis of ALS is when non-motor neuron diseases neurological diseases are considered, as these conditions can mirror ALS's first symptoms[18]. The disease's rarity, lots of variation of disease progression, and difficult prediction and prognosis of the disease due to lack of ALS-specific biomarkers are some of the challenges in ALS diagnosis[19], but due to advanced clinical trials and research, earlier ALS diagnosis is possible. Preclinical technologies, development of biomarkers, early phase trials, and use of advanced statistical analysis with other designs in early phase trials, and gene and stem cell therapies are some opportunities to treat ALS patients[9].

In Africa, the therapy for ALS treatment is done with riluzole. In South Africa, access to riluzole is very constrained. The medication's prohibitive price is the leading cause of this scarcity. Because of this, only a small percentage of ALS patients in South Africa have access to riluzole, potentially depriving them of treatment[6]. Luna *et al.*[20] also observed that only clinics in South Africa, Senegal, Tunisia, and Togo have riluzole on hand. The pricing is inconsistent among nations, making it expensive. Patients have considerable financial hardship to cover the cost.

Risk Factors	Age Gender Family History Trauma Severe hypotonia in children sensory changes Spinal anesthesia Dietary habits smoking drinking alcohol Residence farming occupation Exposure to chemicals
Clinical factors	muscle atrophy (PMA), progressive bulbar atrophy (PBA), progressive bulbar palsy (PBP).
Challenges for Diagnosis	Presence of four classes of Motor Neuron Diseases (MNDs): • ALS, • Primary Lateral Sclerosis (PLS), • Progressive Muscular Atrophy (PMA), • Progressive Bulbar Palsy (PBP)
Management	Use of riluzole

Figure 1. Risk factors, clinical manifestations, diagnosis, and management of amyotrophic lateral sclerosis (ALS) in Africa.

Future directions and research of ALS in Africa

Assessing the incidence of ALS in Africa is hindered by limited data and the absence of population-based registries. Moreover, studies in Africa have mainly focused on populations with similar ancestries, making it challenging to identify environmental and lifestyle risk factors associated with the disease.

Current ALS therapies provide symptomatic relief but lack significant treatment effects. However, there is promising progress in clinical trials investigating various therapeutic strategies. These trials encompass diverse approaches like gene therapy, immunotherapy, and interventions targeting neuroinflammation, phase separation, and protein clearance. Although these interventions are in the early stages of development, they hold great potential for transforming ALS treatment.

Patients attending multidisciplinary ALS clinics demonstrate improved survival compared to those visiting general neurology clinics[21]. These specialized clinics not only enhance care delivery but also enhance the expertise and knowledge of clinicians managing ALS patients, leading to better outcomes. Additionally, technological advancements, such as telehealth services, have facilitated care delivery by providing convenient access to healthcare for ALS patients, positively received by both patients and caregivers.

From an epidemiological standpoint, few studies have been conducted in African countries to determine the incidence and

prevalence of ALS. Future research could help fill these gaps in knowledge. Future research should prioritize well-characterized and optimized clinical trials to identify risk and prognostic factors. Integrating machine learning algorithms with clinical, biofluid, and imaging biomarkers can significantly improve trial design and accuracy. Real-world data analysis is valuable for assessing trial feasibility and designing clinical studies, offering insights for the development of potential ALS treatments.

From a cultural perspective, African cultures may define illness and disability differently from Western cultures, which could affect how patients and their families cope with ALS. Understanding cultural beliefs and practices related to illness could improve support for people living with ALS in African communities.

Collectively, these research efforts will enhance our understanding of ALS by unraveling its underlying mechanisms, including cellular pathogenesis, and opening new avenues for therapeutic possibilities.

From the standpoint of advocacy and awareness, raising awareness about ALS in Africa could help reduce stigma and increase support for patients and their families. Greater advocacy efforts could also drive more funding for research and treatment programs.

Conclusion

ALS is more prevalent in Africa than in developed countries and is often associated with a worse prognosis. On one hand, this is related to environmental factors such as exposure to heavy metals, silica, lead, organic dust, and smoke. On the other hand, it is related to family history and genetic mutations (C9orf72, SOD1, TDP-43, TARDBP, and FUS). Moreover, treatment in Africa is considered very expensive to the population and is poorly available.

Understanding ALS needs advanced research and close monitoring of patients. For example, developing specialized ALS multidisciplinary clinics and providing equal care to all affected patients can help achieve a well-controlled state and improve the knowledge of physicians, thus providing optimal care. In addition, further research is needed to discover and identify specific ALS biomarkers and targeted therapy.

It is not only about scientists' education about ALS, but we also need to target the population. Awareness campaigns for the general population about the disease and risk factors and further education of patients are needed. Treatment should be fairly distributed all over the globe with reduced prices to those who cannot afford it and with very close monitoring of this process to make sure that every patient takes his right to equal care.

We urge African practitioners, researchers, and policymakers to invest more in ALS diagnosis, care, and management to achieve well-controlled states with better prognoses.

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