CLINICAL STUDIES / ETUDE CLINIQUES

ENVIRONMENTAL AND OCCUPATIONAL RISK FACTORS OF AMYOTROPHIC LATERAL SCLEROSIS IN SENEGAL

FACTEURS DE RISQUE ENVIRONNEMENTAUX ET PROFESSIONNELS DE LA SCLEROSE LATERALE AMYOTROPHIQUE AU SENEGAL

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ABSTRACT

Background: The pathophysiology of Amyotrophic lateral sclerosis (ALS) is not well known, but seems to be multifactorial. Genetic and environmental factors increase the risk of developing ALS.

Methods: We conducted case-control study from July 2015 to June 2017, comparing exposure to risk factors in 23 ALS cases and 53 controls in the department of neurology of Fann national teaching hospital in Senegal.

Results: The mean ages of cases and controls were 44.3 ± 16.3 years and 48.3 ± 17 years respectively. There was a male predominance. In the bivariate analysis, factors significantly associated to ALS were: living outside Dakar (OR: 26.6; 95% CI [5.5-127.7]), farmer profession (OR: 13.3; 95% CI [2.6-69.9]), exposure to pesticides (OR: 15.3; 95% CI [3.7-63.4]), and chemical fertilizers (OR: 5.2; 95% CI [1.7-15.4]). In multivariate analysis, living outside Dakar (OR: 16.4; 95% CI [3.2-82.8]) and exposure to pesticides (OR: 6.0; [1.3-29.1]) were identified as the main risk factors of ALS in this study.

Conclusion: We found relatively young ALS patients. This study identified significant role of living outside Dakar and exposure to pesticides. A multi-center study with a larger number of ALS patients would certainly be more accurate in determining more risk factors and their causality in ALS among African population.

INTRODUCTION

Amyotrophic lateral sclerosis (ALS), also known as Charcot's or Lou Gehrig's disease, is a fatal neurodegenerative disease characterized by the loss of motor neurons in the cerebral cortex, brainstem, and spinal cord. ALS causes paralysis of skeletal muscles including respiratory muscles leading to death from respiratory distress. It is the most common motor neuron disease (1). The diagnosis is usually based on clinical and electrophysiological signs. Patients are classified according to the criteria of El Escorial and its revisions (9). The pathophysiology is not well known, but seems to be multifactorial. In fact, about 10 to 15% of patients suffer from the familial form of the disease (familial ALS) while the other patients suffer from the sporadic form (sporadic ALS) (11). Genetic and environmental factors increase the risk of developing ALS (6, 8). The evolution of the disease is fatal with a mean survival of 3 to 5 years after the onset of symptomatology (2).

The growing interest in the study of ALS risk factors around the world contrasts with the few studies conducted in Africa. This work was carried out to determine the environmental and occupational risk factors of ALS in Senegal, a sub-Saharan African country.

MATERIALS AND METHODS

We carried out a case-control age-matched study from July 2015 to June 2017 in the department of neurology of Fann national teaching hospital in Dakar. This department is the main referral center for neurological diseases in Senegal. This study has been approved by the ethical committee of the institution. Cases and controls were included after completing an informed consent form.

Cases and controls recruitment

Cases were incident ALS patients recruited in outpatient consultation based on revised El Escorial criteria (Awaji-Shima) after complete clinical examination and electrophysiological exploration (9). Brain MRI and lab testing (example: FBC, ESR, CRP, fasting blood glucose, thyroid hormone test, liver function test, kidney function test, HIV serology, syphilitic serology, B9 and B12 vitamin dosage, CSF analysis) were performed in all patients to rule out medical conditions mimicking ALS.

The controls were also new patients received in our outpatient consultation with: *(1)* no ALS or MND, *(2)* no neurodegenerative conditions, *(3)* no family history of ALS of frontotemporal dementia.

Since ALS is a rare neurological disease, we choose a ratio: 1 cases / 2.5 controls.

Data collection

A standardized questionnaire was used to collect data from our participant during an interview. These included: *(1)* sociodemographic data such as age, gender, residence location, educational level and profession; *(2)* history of head trauma, smoking, alcohol consumption, electric shock and, exposure to pesticides, chemical fertilizers and X-ray; *(3)* source of drinking water.

Statistical analysis

Statistical tests were carried out using SPSS 23.0 for Windows®. The results were expressed in frequency and mean with standard deviation. We performed a bivariate analysis by calculating the odds ratio (OR) with a 95% confidence interval (CI). Variables significantly associated were introduced in the multivariate analysis using linear logistic regression. We determined factors significantly associated to ALS independently from other factors. ALS was our dependent variable, and other were independents. The results were statistically significant for a $P < 0.05$.

RESULTS

We collected 76 participants including 23 ALS cases and 53 controls.

Bivariate analysis

Sociodemographic data

The mean age of cases was 44.3 ± 16.3 years with extremes of 16 to 70 years. The mean age of controls was 48.3 ± 17 years with extremes of 17 to 72 years. There was no statistically significant difference between the age of ALS patients and controls ($p < 0.840$). ALS patients and controls were predominantly male, representing 65.2% and 54.7% respectively. No gender was associated to ALS occurrence. Among ALS patients, 91.3% lived out of Dakar region. Living outside Dakar was significantly associated to ALS ($p < 0.001$). In the case group, 34.8% were farmer whereas 3.8% in the control group. Work as farmer was significantly associated to ALS ($p = 0.001$) (*table 1*).

Medical history and exposure

Exposure to pesticides and chemical fertilizers were found in 47.8% and 52.2% of ALS patients respectively. While these exposures were found in 5.7% and 17% of controls respectively. Pesticides ($p < 0.001$) and chemical fertilizers ($p = 0.004$) were significantly associated to ALS (*table 2*).

Sources of drinking water

The sources of drinking water for ALS patients were: tap water (91.3%), well water (21.7%) and mineral water (4.3%). In the control group, the sources were tap water (86.8%), well water (7.5%) and mineral water (9.4%). No source of water was associated to the development of ALS (*table 2*).

Multivariate analysis

After identifying different factors significantly associated to ALS in bivariate analysis, we performed a linear logistic regression analysis to determine independent factors significantly associated to development of ALS. We found two independent factors which constituted the risk factors of ALS in Senegal: living outside Dakar ($P = 0.001$) and exposure to pesticides ($P = 0.025$) (*table 3*).

DISCUSSION

The main limitation of this study was the reduced number of ALS cases. This make the analysis difficult.

Age and gender

The mean age of patients at the time of diagnosis is about 58 to 63 years for sporadic ALS and 47 to 52 years for familial ALS (9). In Africa, studies usually reported a young age of ALS patients (10). The most recent study conducted in Senegal found a median age of 50 years old in 33 cases of sporadic ALS (12). ALS is most frequent in male than female with a sex ratio of 1.5: 1 (3). In Africa most studies found male predominance with sex ratio up to 17 (10).

Residence location

Certain regions have been associated to high prevalence of ALS. In Nigeria, 18.7% of patients resided in the Warri zone in the Niger Delta oil region (5). For Das et al, rural life was significantly associated with the occurrence of ALS with OR: 1.99, 95% CI [1.02 – 3.88] (4). Between 1972 and 1988, the municipality of Reggio Emilia (northern Italy) was associated with a high risk of ALS (14). On the island of Guam in the Pacific, consumption of BMAA toxin was associated with a high incidence of ALS (6). Dakar is the main city and the most developed region of Senegal. Patients living outside Dakar are more likely to be in semi-urban or rural area.

Farmer

Agriculture and livestock were found in 2.7% of ALS patients in the United States (11). In India, agriculture was not associated with a significant risk of developing ALS, according to Das et al, in 2012 (OR: 1.07, 95% CI [0.62 – 1.85]) (4). The use of pesticides and chemical fertilizers increases the risk of ALS among farmers (6, 15). In Senegal, farmers are predominantly located in rural area.

Pesticides and chemical fertilizers

Several studies have found a significant risk associated to the use of pesticides (6, 7, 8, 13). Yu et al, found a significant association between pesticide exposure in the previous 30 years and the occurrence of ALS with an OR of 6.95, 95% CI [1.23-39.1] (15). The pesticides implicated in ALS development are organochlorides (including dichloro-diphenyl-trichloroethane), herbicides, pyrethroids, and fumigants (13). Chronic exposure to organophosphates, the most widely used herbicides in the United States, causes irreversible brain damage by inhibiting acetylcholinesterase (13). ALS patients would be unable to eliminate the organophosphates of their organism due to a mutation of the paraoxonase gene (PON1). Thus, promoting excessive stimulation of cholinergic receptors and excitotoxicity (7, 13).

Few studies focus on the use of chemical fertilizers as a risk factor for ALS. Yu et al, found a significant risk in 2014 for people who used chemical fertilizers in their garden in the previous 10 to 30 years (OR = 2.97, 95% CI [1.01 – 8.76]) (15).

Drinking water

Water is not a risk factor for ALS, but is a source of intoxication. The high risk of ALS in the municipality of Reggio Emilia was associated to high selenium content in tap water (14).

CONCLUSION

In this case control study conducted to determine risk factor for ALS, we found relatively young ALS patients mostly male. We identified significant role of living outside Dakar, farmer activity, exposure to pesticides and fertilizers. The risk factors found were living outside Dakar and exposure to pesticides. A multi-center study with a larger number of ALS patients would certainly be more accurate in determining more risk factors and their causality in ALS among African population.

Disclosure of interest

The authors declare that they have no competing interest.

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TABLES :

Table 1: sociodemographic characteristics of ALS patients and control group.

Variables		Case	Control	Crude OR (95% CI)	P-value
Age		44.3	48.3	–	0.84
Male		15	29	1.5 [0.6 – 4.2]	0.455
Female		8	24	0.6 [0.2 – 1.8]	0.455
Residence location					
	Dakar city	1	18	0.9 [0.01 – 0.7]	0.008
	Dakar suburb	1	20	0.07 [0.009 – 0.6]	0.002
	Outside Dakar	21	15	26.6 [5.5 – 127.7]	<0.001*
Profession					
	Farmer	8	2	13.6 [2.6 – 71]	0.001*
	Tailor	3	1	7.8 [0.8 – 79.5]	0.08
	Professional athlete	1	1	2.4 [0.1 – 39.5]	0.51
	Electrician	1	2	1.2 [0.1- 13.5]	1
	Building Professional	1	3	0.8 [0.07 – 7.7]	1
	Housewife	9	16	1.5 [0.5 – 4.1]	0.596

	Student	1	4	0.6 [0.06 – 5.2]	1
	Administrative employee	1	–	–	–
	Street vendor	1	2	1.2 [0.1 – 13.5]	1
	Driver	1	1	2.4 [0.1 – 39.5]	0.516
	Unemployed	2	2	2,4 [0.3 – 18.4]	0.582
Educational level					
	University	3	4	1.8 [0.4 – 8.9]	0.43
	High school	1	15	0.1 [0.01 – 0.9]	0.03
	Primary school	9	11	2.5 [0.8 – 7.1]	0.15
	Unschooled	10	22	1.1 [0.4 – 2.9]	1

**** Variable significantly associated to ALS (P < 0.05). Frequency of case's profession > 23 because some patients had more than 1 profession.***

Table 2: medical history and exposure of ALS patients and control group.

Variables	Case	Control	Crude OR (95% CI)	P-value
Head trauma	4	8	1,2 [0,3 – 4,4]	1
Electric shock	3	6	1,1 [0,3 – 5,0]	1
Smoking	4	6	1,6 [0,4 – 6,5]	0,48
Alcohol	2	1	4,9 [0,4 – 57,6]	0,22
Pesticides	11	3	15,3 [3,7 – 63,4]	<0,001*
Chemical fertilizers	12	9	5,2 [1,7 – 15,4]	0,004*
X-ray	4	10	0,9 [0,2 – 3,2]	1
Tap water	21	46	1,6 [0,3 – 8,3]	0,71
Well water	5	4	3,4 [0,8 – 14,0]	0,12
Mineral water	1	5	0,4 [0,05 – 3,9]	0,661

**** Variable significantly associated to ALS (P < 0.05)***

Table 3: risk factors of ALS identify after linear logistic regression analyzes

Variables	Adjusted OR (95% CI)	P-value
Outside Dakar	16.4 [3.2-82.8]	0.001
Pesticides	6.0 [1.3-29.1]	0.025

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