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Epidemiological and Clinical Profile of Amyotrophic Lateral Sclerosis in Ethiopia: A 5-year multicenter retrospective study

Dereje Melka MD [*1], Hanna Demisse MD[1], Hanna Assefa MD[1],Yared Zenebe, MD[1], Biniyam A. Ayele MD [1], Meron Awraris, MD[1], Yohannese Gelan , MD[1],Selam Kifelew,MD[1], Medina Fedlu, MD[1],Fikiru Tsehayneh MD[1], Mehila Zebenigus MD[2], Samson Alemayehu MD[2], Heera Tesfaye, MD[3], Hildana Gulelat, MD[3], Tsega Guta MD[3], Abenet Tafesse MD [4], Nebiyu Bekele MD[5], Marc Saez, PhD[6], Jan H. Veldink PhD [7], Ammar Al-Chalabi PhD[8], Monica Povedano PhD[9] , Ahmad Al Khleifat PhD[8].

[1] Assistant professor of Neurology, Department of Neurology,
College of Health Sciences, Addis Ababa University
[2]Assistant professor of neurology, Yehuleshet specialty clinic
[3]General practitioner, Yehuleshet specialty clinic
[4]Associate professor of Neurology, Department of Neurology,
College of Health Sciences, Addis Ababa University
[5]Assistant professor of Neurology, Department of internal medicine neurology unit, college of health science, University of Gondar.
[6] Full Professor of Statistics and Econometrics, Research Group on Statistics, Econometrics and Health (GRECS), University of Girona, Spain, and CIBER of Epidemiology and Public Health (CIBERESP), Spain
[7] Professor of Neurology Department of Neurology, UMC Utrecht Brain Center, Utrecht University, The Netherlands
[8]Professor of Neurology and Complex Disease Genetics, King's College London, Department of Basic and Clinical, Neuroscience, Maurice Wohl Clinical Neuroscience Institute, London SE5 9RS, UK
[9] Professor of Neurology, Department of Neurology, Bellvitge University Hospital, Spain.
[8]Fellow in Clinical Neuroscience, King's College London, Department of Basic and Clinical Neuroscience, Maurice Wohl Clinical Neuroscience Institute, London SE5 9RS, UK

*****Corresponding Author: Dereje Melka
Mailing address Addis Ababa Ethiopia, email address m.dereje@yahoo.com, Telephone +251946375704.

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Abstract

Background: Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease that results in progressive weakness of skeletal muscles including respiratory muscles. Epidemiological and clinical aspects of ALS are derived from a few world regions with very little representation of low- and middle-income countries. We therefore set out to determine the epidemiological and clinical phenotype of individuals with ALS in Ethiopia

Methods: Multicenter retrospective analysis was conducted using clinical records from ALS patients seen in Ethiopia at Tikur Anbessa Specialized Hospital and Yehuleshet specialty clinic between January 2016 and August 2021. The data collected included clinical characteristics, disease-related symptoms, revised ALS functional rating scale, and medications.

Results: Patients in Ethiopia had a younger age of onset with a mean age of disease onset of 51.9 years. 2.9% of patients had juvenile ALS, and the male to female ratio was almost 2:1. 4.9% had a positive family history of the disease. 68% of patients had spinal region involvement at onset, while 32% had bulbar region involvement at onset. Riluzole was used by 31% of ALS patients. 20.6% of patients had some respiratory symptoms, but none received a standard respiratory function assessment. 33.3% of patients were wheelchair-bound.

Conclusion: In this retrospective study spanning 5 years, we examined the clinical phenotype of ALS in Ethiopian patients. Our findings suggest that most patients had clinically definite ALS with spinal region involvement. Further research, including genetic and epigenetic information, is necessary to understand the early onset of the disease in Ethiopia.

Introduction

Amyotrophic lateral sclerosis (ALS), also known as motor neuron disease, is a neurodegenerative disorder that causes progressive weakness in the muscles that control movement and breathing (1,2). The incindence of ALS is approximately 1 – 2.6 cases per 100,000 person-years and a prevalence of about 6 cases per 100,000 persons(3). However, the lifetime risk of developing ALS is about 1 in 300 by the age of 80, which is similar to the risk of multiple sclerosis in the UK and Ireland (4,5).

There is a significant diagnostic delay in ALS, typically about a year, which seems to be independent of the healthcare system and is probably related to low recognition by primary care physicians(6,7). As a result, those attending specialist centers tend to be those with a better prognosis, who are younger, and who are more motivated(8).

Two studies project an increase in the number of people newly diagnosed with ALS across the globe. For example, one estimate is that numbers will increase from 222,801 in 2015 to 376,674 in 2040, representing an increase of 69%. This increase is mainly due to the aging of the population, particularly among developing nations(9,10)

Most of the data on the epidemiological and clinical aspects of ALS is derived from a few world regions, and very little is known about ALS in low and middle-income countries, in particular, East and Sub-Saharan Africa, and data from the region is limited to clinical series or case reports. In addition, data from low and middle-income countries could potentially deliver important information regarding the etiology of ALS, as there are significant differences when considering environmental conditions and lifestyle factors between low and middle-income countries and high-income countries(11)

Ethiopia is a country in East Africa with a population of around 120.3 million people, making it the second most populous country in Africa. The healthcare system in Ethiopia is organized into three levels of publicly funded healthcare services: primary care, secondary care, and tertiary care. Within this system, Tikur Anbessa specialized hospital operates outpatient neurology clinics seven

days a week. Among these clinics, there is a dedicated clinic for neuromuscular junction disorders, where patients with ALS are evaluated. On a daily basis, the neuromuscular disorder clinic assesses 20-30 patients with neuromuscular junction disorders. Yehuleshet Speciality Clinic, on the other hand, is a private clinic primarily catering to patients with neurological disorders. It handles a significant number of cases related to neurological disorders 12. In line with this, we have undertaken a study to investigate the epidemiological and clinical characteristics of individuals diagnosed with amyotrophic lateral sclerosis in Ethiopia. The study covers the period from January 2016 to August 2021, aiming to better understand the specific features of ALS in the Ethiopian population.

Methods

The study was conducted at Tikur Anbessa Specialized Hospital and Yehuleshet Specialty clinic. Both health institutions provide health services for people living in and near Addis Ababa, as well as people referred from other regions in Ethiopia.

An institutional cross-sectional study was conducted between January 2016 and August 2021. Clinical data were collected using a structured questionnaire which included demographic information, a detailed clinical history, physical findings, and treatment outcomes of people with ALS (supplementary appendix). Revised ALS functional rating scale (ALSFRS-R) was assessed on the last patient vist, and El Escorial criteria for the diagnosis of ALS were also assessed(13–17). The questionnaires were administered by neurologist. The clinical information obtained from patient recordsa and through patient interviews via phone.

Analysis was performed using SPSS version 25.0 (SPSS Inc., Illinois, USA) for statistical analysis. Descriptive summaries were employed to describe socio-demographic and clinical characteristics. Fisher's Exact test was used for pairs of categorical variables, and binary logistic regression analysis for dependent binary categorical variables. Odds ratios and 95% confidence intervals were calculated. For mortality statistics, because disease duration and censoring data were incomplete, chis-squared tests or logistic regression were used to test for an increase in reported deaths over the expectation for categorical variables.

Protocol approvals were obtained from the Ethical Review Committee of the Department of Neurology and the Institutional Review Board and the Research and Publication Committee of the College of Health Sciences of Addis Ababa University. Participants' names and other identifiers were not included, to maintain confidentiality.

Results

Baseline characteristics of the study participants

102 people with ALS were studied. The mean age of onset was 51.9 years (SD 14.1). The mean age of onset for males was 52.43 years and for females 50.16 years. 69.6% (n=71) of the population was male. Juvenile ALS, defined by an age of onset of less than 25 years, was observed in three individuals, two male and one female. The age of onset for the male patients was 20 and 21 years, and for the female patient, it was 23 years. None of them was related, and no family history of a similar illness was reported.

Of the 102 people assessed, 5 (4.9%) reported a family history of ALS. A family history of ALS was associated with a younger age at onset (49.2 years, 95% CI 0.37 to 5.96 years). El Escorial "definite" ALS accounted for 56.9% of the study participants, followed by "clinically probable" ALS (22.5%). Only one person was diagnosed with frontotemporal dementia in this study.

Diagnostic Delay

On average the median diagnostic delay was about 2 years (SD 1.82), 1.95 years for males, 2.06 years for females.

Site of Onset

At onset 68% of the patients showed evidence of spinal region involvement and 32% of patients showed evidence of bulbar region involvement.

Functional impairment

60.8% of participants reported speech disturbance. Six (5.9%) had marked drooling and 67.6% some degree of swallowing difficulty (Table 2). In handwriting assessment, 15.7% (n=16) were unable to grip a pen. 23 (22.6%) were dependent on family members for dressing and hygiene. 22 (21.5%) reported shortness of breath and 10 (9.9%) participants reported Respiratory distress (Table 2).

Access to Care and Thereapy

93.1% of the participants had only one visit to health facilities. 46.5% (n=40/86) received motor rehabilitation therapy, 6.3% (n=4/64) received speech therapy, and 31% (n=26/84) were treated with Riluzole (Table 1). One patient required non-invasive ventilation and only one patient required gastrostomy.

Factors associated with ALS mortality in the study participants

Mortality tested against various characteristics is reported in Tables 4 and 5 .

Discussion

We have provided a detailed description of ALS in Ethiopia. ALS patients had a younger age of onset than usually reported in European or US studies, with a mean age of disease onset of 51.85 (±14.2) years (18). This is comparable with a study from Tunisia, which showed a mean age of disease onset of 54.93 (±14.08) years (19), and anotherin South Africa in which South African ALS patients had a younger age of onset than their Portuguese counterparts (11). Studies from Egypt and Senegal also report a mean age of onset of 49.2 (±15.1) years (20) and 44.3 (±16.3) years (21), respectively. North African ALS patients are significantly younger than is seen in European studies (22,23). For example, a study in Italy reported a higher mean age of ALS patients (64.8 ± 11.2 years) than the present study (24), as does a study from Germany reporting a mean age of onset of 66.2 ± 10.3 years (25). This indicates that African ALS patients have a younger mean age than those in Europe. However, this observation might be due to an epidemiological artefact because a younger median age in the Ethiopian population by necessity drives down the median age of age-related diseases like ALS and the variation in the life expectancy of the population, and this trend of an association between life expectancy and mean age of ALS onset is seen globally (26)

Young onset ALS (below age 25) was seen in 2.9% (3/102) of patients which is lower than reported in Tunisia 5.71% (12/210) (27). This difference is likely related to sampling variance.

The male to female ratio in this study was nearly 2:1. This is comparable to a study from Egypt which reported a male to female ratio of 3:1 (20). Similar findings have been reported in studies from Senegal and Tunisia, where males are predominant (19,21). These ratios likely represent the younger population in lower and middle income countries because of access to care and the change in sex ratio by age; in support of this conjecture, reports from European datasets indicate a more equal distribution between males and females, consistent with the older age of onset in these populations, as older patients are more likely to be female.

In most cases, ALS occurs sporadically, with only around 5% of patients having a positive family history of the disease (28). In the present study, a similar finding was identified, with a positive family history of ALS seen in 4.9% of our patients. A nearly comparable report was also observed in Ireland, where 7% of patients had a positive family history of ALS (29). However, this may be explained by differences in family size and the definition of a positive family history (30,31).

Based on the El Escorial criteria for the diagnosis of ALS, the present study showed definite ALS (56.9%), probable ALS (22.5%), and possible ALS (20.6%). This finding is almost comparable to a report from Ireland, which reported definite ALS (67%), probable ALS (19%), and possible ALS (12%) (29), and similar findings have also been reported from Italy (32,33).

The mean time delay from onset to diagnosis was about 2 years (SD 1.82), in comparison to the higher mean diagnostic delay was reported in Tunisian ALS patients (2.41 (SD 4.48) years) (19). This could be due to recall bias in the current study. However, a study from Italy reported a mean time delay from onset to diagnosis of 10.4 (SD10.1) months (24), which is less than the present study.

Spinal involvement at onset was seen in 68% of patients, and bulbar region involvement at onset was seen in 32% of patients, findings similar to those reported elsewhere including in a Tunisian study, 77.61% and 19.04% respectively (19).

In our study, 31% (26 out of 84 ALS patients) used Riluzole. This is higher than for South African ALS patients, but lower compared to Portuguese ALS patients (11). This difference in different parts of the world is likely related to healthcare systems and availability of medication.

Non-invasive positive pressure ventilation (NPPV) has been shown to provide clear benefits in ALS patients, including prolonged survival when initiated early (34)(35). In our study, 20.6% of

patients reported respiratory symptoms, but none underwent a standard respiratory function assessment. Only one patient received NPPV, likely due to limited availability and financial constraints faced by most Ethiopian ALS patients.

The present study showed that 33.3% of patients were wheelchair-bound. A study from Italy also showed a comparable finding that 25.4% of the patients were wheelchair-bound (36).

Our study found a high mortality rate among ALS patients, with 47.5% (29 out of 61) of patients assessed during follow-up having died. This aligns with a study from South Africa that reported higher mortality rates compared to their Portuguese counterparts (11). A study from Taiwan also reported similar mortality rates (37). Despite younger age and mostly spinal onset ALS in our patients, typically associated with better outcomes (25) (38), our study still observed higher mortality. This suggests limited healthcare access due to economic reasons for our ALS patients.

Our study had several limitations. The study is retrospective in design and a few of the patient charts and electrophysiology result reports were incomplete. Our findings might not be generalizable because they only included patients from two clinical services located in the same city. However, we are likely to have captured most people with ALS within our catchment area.

During the retrospective data collection process, we discovered that a patient had been diagnosed with dementia. However, the specific subtype of dementia was not recorded. Additionally, we were unable to contact most of the patients using the phone numbers listed on their charts. As for genetic screening for ALS, due to limited resources we were not able to perform such tests on our patients. The age of death was not recorded in our data, we were not able to perform survival analysis.

There were no significant differences in mortality outcomes observed among individuals receiving Riluzole, speech therapy, and rehabilitation, likely due to the limitations in our study design. Cross-sectional analysis provides a snapshot of a specific moment, allowing for the assessment of prevalence and associations, but it cannot establish causality or evaluate the evolution of variables over time.

The main strength of this study is that it reports details of the clinical phenotype of ALS in Ethiopian patients and associated factors and will act as a foundation for future studies.

In summary, our study has provided important insight into the prevalence and clinical phenotype of ALS in Ethiopian patients, where the majority were diagnosed with clinically definite ALS and presented with spinal region involvement. To understand the reasons for the early onset of the disease in Ethiopia, further research incorporating genetic and epigenetic information is necessary.

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Competing Interests

AAC is a consultant for Mitsubishi-Tanabe Pharma, GSK, and Chronos Therapeutics, and chief investigator for clinical trials for Cytokinetics and OrionPharma. JHV reports to have sponsored research agreements with Biogen, grants from The European Community's Health Seventh Framework Programme (grant agreement n° 259867 (EuroMOTOR)), grants from The Netherlands Organization for Health Research and Development)the STRENGTH project, funded through the EU Joint Programme – Neurodegenerative Disease Research, JPND), during the conduct of the study; personal fees from Calico, personal fees from Cytokinetics, grants and personal fees from Takeda, non-financial support from Orion, non-financial support from Orphazyme, outside the submitted work. The rest of the authors declare no competing interests.

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Tables

Table 1: Baseline characteristics & clinical outcomes of the study participants (N=102)

Variables	**Frequency (%)**
Age in years (mean, SD)	51.9 (13.6)
Sex	
Male	71 (69.6)
Female	31 (30.4)
Educational status	
No formal/ or below primary education	52 (51)
Secondary education and above	50 (49)
Occupational status	
Employed	31 (30.4)
Unemployed	71 (69.6)
Family history of ALS	
Yes	5 (4.9)
No	97 (95.1)
Mobility	
Walking	68 (66.7)
Wheelchair bounded	34 (33.3)
Frequency of hospital visits after ALS diagnosis	
Below 2 visits	95 (93.1)
3 visits and above	7 (6.9)
Clinical outcomes (n=61)*	
Deceased	29 (52.5)
Alive	32 (47.5)

Classification of ALS (El Escorial & Awajii Criteria)	
Clinically definite ALS	58 (56.9)
Clinically probable ALS	23 (22.5)
Probable ALS–Laboratory Supported	10 (9.8)
Clinically possible ALS	11 (10.8)
Treatment	
Motor rehabilitation (n=86)*	40 (46.5)
Speech therapy (n=64)*	4 (6.3)
Riluzole (n=84)*	26 (31)

Table 2: Revised ALS functional rating scale (ALS-FRS-R) of the study participants on the last institution visit (N=102)

	Frequency (%)
Speech	
Normal speech process	26 (25.5)
Detectable speech disturbance	35 (34.3)
Intelligible with repeating	16 (15.7)
Speech combined with non-vocal communication	6 (5.9)
Loss of useful speech	5 (4.9)
No documents	14 (13.7)
Salivation	
Normal	47 (46.1)
Slight but definite excess of saliva in mouth; may have nighttime drooling	19 (18.6)
Moderately excessive saliva; may have minimal drooling	5 (4.9)

Marked excess saliva with some drooling	3 (2.9)
Marked drooling	6 (5.9)
Not documented	22 (21.6)
Swallowing	
Normal eating habits	33 ((32.4)
Early eating problems –occasional choking	50 (49)
Dietary consistency changes	14 (13.7)
Needs supplemental tube feeding	4 (3.9)
Nothing by Mouth (NPO)	1 (1)
Handwriting	
Normal	21 (20.6)
Slow or sloppy: all words are legible	7 (6.9)
Not all words are legible	1 (1)
No words are legible, but can still grip the pen	4 (3.9)
Unable to grip pen	16 (15.70
Not documented	53 (52)
Cutting food and handling utensils (without gastrostomy)	
Normal	24 (23.5)
Clumsy, but able to perform all manipulations independently	1 (1)
Somewhat slow and clumsy, but no help needed	15 (14.7)
Can cut most foods (> 50%), although slow and clumsy; some help needed	4 (3.9)
Food must be cut by someone, but can still feed slowly	7 (6.9)
Needs to be fed	22 (21.6)
Not documented	29 (28.4)

Cutting food and handling utensils (with gastrostomy)	
Normal	3 (2.9)
Clumsy, but able to perform all manipulations independently	12 (11.8)
Some help is needed with closures and fasteners	3 (2.9)
Provides minimal assistance to the caregiver	2 (2)
Unable to perform any aspect of a task	1 (1)
Not documented	81 (79.4)
Dressing and Hygiene	
Normal function	23 (22.5)
Independent; Can complete self-care with effort or decreased efficiency	9 (8.8)
Intermittent assistance or substitute methods	9 (8.8)
Needs attendant for self-care	9 (8.8)
Total dependence	23(22.6)
Not documented	29 (28.4)
Turning in bed and adjusting bedclothes	
Normal function	24 (23.5)
Somewhat slow and clumsy, but no help needed	11 (10.8)
Can turn alone, or adjust sheets, but with great difficulty	6 (5.9)
Can initiate, but not turn or adjust sheets alone	8 (7.8)
Helpless	19 (18.6)
Not documented	34 (33.3)
Walking	
Normal	30 (29.4)
Early ambulation difficulties	24 (23.5)

Walks with assistance	12 (11.8)
Non-ambulatory functional movement only	18 (17.6)
No purposeful leg movement	8 (7.9)
Not documented	10 (9.8)
Climbing stairs	
Normal	22 (21.6)
Slow	16 (5.7)
Mild unsteadiness or fatigue	5 (4.9)
Needs assistance	4 (3.9)
Cannot do	25 (24.5)
Not documented	30 (29.4)
Dyspnea	
None	55 (53.9)
Occurs when walking	9 (8.8)
Occurs with one or more of the following: eating, bathing, dressing	2 (2)
Occurs at rest: difficulty breathing when either sitting or lying	9 (8.8)
Significant difficulty: considering using mechanical respiratory support	2 (2)
Not documented	25 (24.5)
Orthopnea	
None	58 (56.9)
Some difficulty sleeping at night due to shortness of breath does not routinely use more than two pillows	2 (2)
Needs extra pillows to sleep (more than two)	5 (4.9)
Can only sleep sitting up	2 (2)

Unable to sleep without mechanical assistance	1 (1)
Not documented	34 (33.3)
Respiratory insufficiency	
None	58 (56.9)
Intermittent use of BiPAP	0 (0)
Continuous use of BiPAP during the night	1 (1)
Continuous use of BiPAP during day & night	0 (0)
Invasive mechanical ventilation by intubation or tracheostomy	1 (1)
Not documented	42 (41.2)

Table 3: Site of onset (N=102)

Site of onset	**Frequency (%)**
Bulbar region	
Unaffected	25 (24.5)
Affected on examination only (accepted signs: tongue atrophy fasciculation, slowness of movement)	74 (72.5)
Affected on reflex examination only (accepted sign: pathologically brisk jaw jerks only)	3 (2.9)
Upper limbs	
Unaffected	14 (13.7)
Function affected (e.g. difficulty with keys, doorknobs, zips, bags)	71 (69.6)
Affected on examination only (accepted sign: wasting of the first dorsal interossei)	1 (1)
Affected on reflex examination only (accepted signs: the presence of pectoral reflexes or Hoffman's sign)	16 (15.7)
Lower limbs	

Unaffected	26 (25.5)
Function affected e.g. difficulty walking, falls, cramps, etc.	52 (51)
Affected on examination only (accepted signs: gait stiffness or foot drop)	19 (18.6)
Affected on reflex examination only (accepted signs: crossed adductor reflexes, pathologically brisk patellar reflexes, or ankle clonus)	5 (4.9)
Respiratory symptoms	
Yes	21 (20.6)
No	56 (54.9)
Not documented	25 (24.5)
Respiratory function not documented	102 (100)

Table 4: Association between clinical outcomes and characteristics of study participants

Variables	**Outcomes**		**P value**
	Alive N=32/61 (52.5%)	**Deceased N=29/61 (47.5%)**	
Age category			
Below 54 years	20 (32.8)	14 (23)	0.26
Above 54 years	12 (19.7)	15 (24.6)	
Sex			
Male	16 (26.2)	24 (39.3)	0.007
Female	16 (26.2)	5 (8.2)	
Employment			
Employed	7 (11.5)	13 (21.3)	0.07
Unemployed	25 (41)	16 (26.2)	

Educational status			
Above secondary education	6 (9.8)	9 (14.8)	0.57
Secondary education only	11 (19)	6 (9.8)	
Primary education only	8 (13.1)	7 (11.5)	
No formal education	7 (11.5)	7 (11.5)	
Family history of ALS			
No	29 (47.5)	27 (44.3)	0.73
Yes	3 (4.9)	2 (3.3)	
Received motor rehabilitation			
No	13 (22)	17 (28.8)	0.24
Yes	17 (28.8)	12 (20.3)	
Received speech therapy			
No	23 (51.1)	18 (40)	0.62
Yes	3 (6.7)	1 (2.2)	
Received Riluzole therapy			
No	22 (39.3)	20 (35.7)	0.87
Yes	7 (12.5)	7 (12.5)	

Table 5: Logistic regression analysis of ALS mortality and covariates in the study participants

	COR	**95% CI**	**p-value**	**AOR**	**95% CI**	**p-value**
Age category						
Below 54 years	Ref.					
Above 54 years	0.56	0.20 – 1.56	0.27	0.44	0.13 – 1.46	0.18
Sex						

Female	Ref.					
Male	0.21	0.06 – 0.68	0.01	0.19	0.06 – 0.66	**0.009**
Employment						
Employed	Ref.					
Unemployed	2.90	0.95 – 8.83	0.06	2.41	0.61 – 9.58	0.21
Received motor rehabilitation						
No	Ref.					
Yes	1.85	0.66 – 5.21	0.24	1.32	0.38 – 4.61	0.66

¶ COR: Crude odds ratio; AOR: Adjusted odds ratio; CI: Confidence interval.

Figures

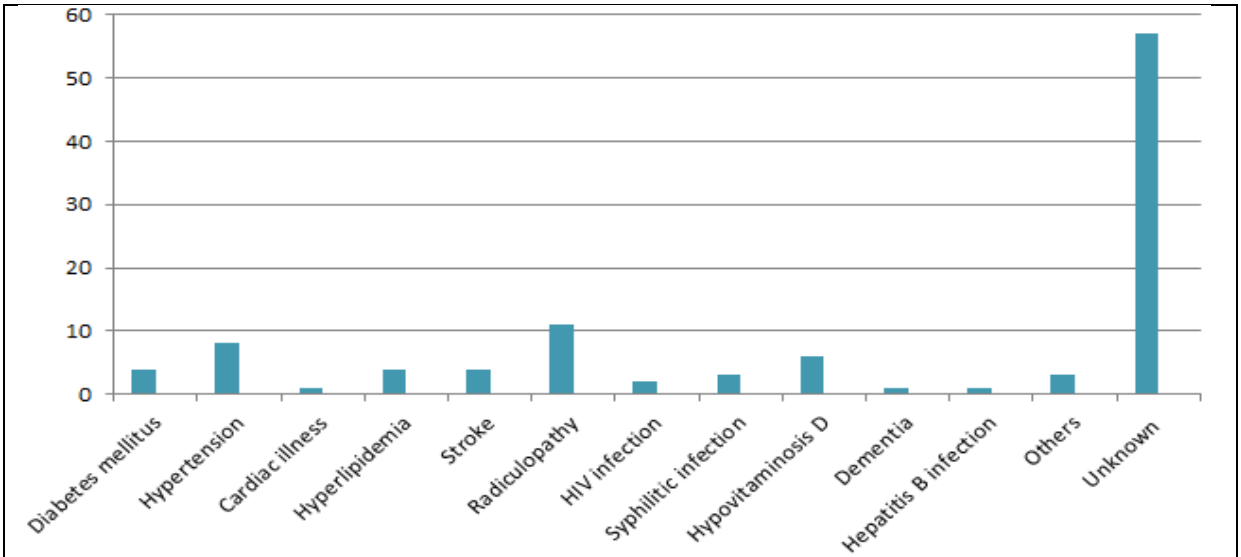

Figure 1: Bar graph showing the distribution of comorbid disorders in ALS Ethiopian patients

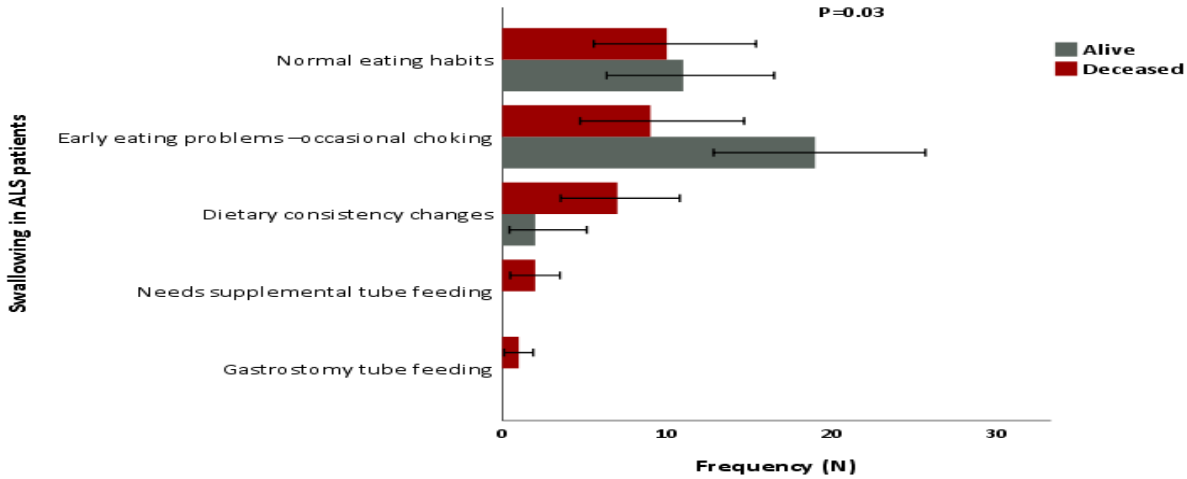

Figure 2: Bar graph showing swallowing difficulty was associated with mortality in the study participants

Suplmentery appendix

Study Questionnaire:

Part I: Background (socio demographic) characteristics

1. Name of the health facility :_____
2. Patient identification number:_____
3. Age:_____(in years)
4. Age at onset of the illness:_____(in years)
5. Age at diagnosis:_____ (in years)
6. Gender:
    a. Male ☐
    b. Female ☐
7. Handedness:
    a. Right ☐
    b. Left ☐
8. Occupational status:
    a. Employed ☐
    b. Unemployed ☐
9. Educational status:
    a. No formal education ☐
    b. Primary education ☐

c. Secondary education ☐

d. More than secondary education ☐

10. Marital status:

a. Married □

b. Not married □

c. Widow □

d. Divorced □

11. Family history of similar illness:

a. Yes ☐

b. No ☐

12. If the answer to Q11 is yes, specify the relationship with the patient:_____

13. History of consanguinity:

a. Yes ☐

b. No ☐

14. Mobility:

a. Walking ☐

b. Wheelchair ☐

15. Comorbidities:

a. Yes ☐

b. No □

16. If the answer to Q16 is yes, specify:_____

17. Frequency of visit at the neurology outpatient department:_____

Part II: Revised ALS functional rating scale (**ALS-FRS-R)**

No	**Item**	**Score**
1	**Speech**	Not documented □
	Normal speech process	4
	Detectable speech disturbance	3
	Intelligible with repeating	2
	Speech combined with non-vocal communication	1
	Loss of useful speech	0
2	**Salivation**	Not documented □
	Normal	4
	Slight but definite excess of saliva in mouth; may have night time drooling	3
	Moderately excessive saliva; may have minimal drooling	2
	Marked excess of saliva with some drooling	1
	Marked drooling	0

3	**Swallowing**	Not documented □
	Normal eating habits	4
	Early eating problems –occasional choking	3
	Dietary consistency changes	2
	Needs supplemental tube feeding	1
	NPO	0
4	**Handwriting**	Not documented □
	Normal	4
	Slow or sloppy: all words are legible	3
	Not all words are legible	2
	No words are legible, but can still grip pen	1
	Unable to grip pen	0
5a	**Cutting food and handling utensils (without gastrostomy)**	Not documented □
	Normal	4
	Somewhat slow and clumsy, but no help needed	3
	Can cut most foods (> 50%), although slow and clumsy; some help needed	2
	Food must be cut by someone, but can still feed slowly	1

	Needs to be fed	0
5b	**Cutting food and handling utensils (with gastrostomy)**	Not documented □
	Normal	4
	Clumsy, but able to perform all manipulations independently	3
	Some help needed with closures and fasteners	2
	Provides minimal assistance to caregiver	1
	Unable to perform any aspect of task	0
6	**Dressing and hygiene**	Not documented □
	Normal function	4
	Independent; Can complete self-care with effort or decreased efficiency	3
	Intermittent assistance or substitute methods	2
	Needs attendant for self-care	1
	Total dependence	0
7	**Turning in bed and adjusting bed clothes**	Not documented □
	Normal function	4
	Somewhat slow and clumsy, but no help needed	3
	Can turn alone, or adjust sheets, but with great difficulty	2

	Can initiate, but not turn or adjust sheets alone	1
	Helpless	0
8	**Walking**	Not documented □
	Normal	4
	Early ambulation difficulties	3
	Walks with assistance	2
	Non-ambulatory functional movement only	1
	No purposeful leg movement	0
9	**Climbing stairs**	Not documented □
	Normal	4
	Slow	3
	Mild unsteadiness or fatigue	2
	Needs assistance	1
	Cannot do	0
10	**Dyspnea**	
	None	4
	Occurs when walking	3

	Occurs with one or more of the following: eating, bathing, dressing	2
	Occurs at rest: difficulty breathing when either sitting or lying	1
	Significant difficulty: considering using mechanical respiratory support	0
11	**Orthopnea**	Not documented □
	None	4
	Some difficulty sleeping at night due to shortness of breath, does not routinely use more than two pillows	3
	Needs extra pillows in order to sleep (more than two)	2
	Can only sleep sitting up	1
	Unable to sleep without mechanical assistance	0
12	**Respiratory insufficiency**	Not documented □
	None	4
	Intermittent use of BiPAP	3
	Continuous use of BiPAP during the night	2
	Continuous use of BiPAP during day & night	1
	Invasive mechanical ventilation by intubation or tracheostomy	0
	Abbreviation: Revised ALS Functional Rating Scale (ALSFRS-R, BiPAP Bilevel positive airway pressure	

Part III: KING'S ALS STAGING

No	Area Involved	
1	**Bulbar region:**	
	Unaffected	□
	Function affected (e.g. slurred speech, slowing difficulty, or hypophonia)	□
	Affected on examination only (accepted signs: tongue atrophy fasciculation, slowness of movement)	□
	Affected on reflex examination only (accepted sign: pathologically brisk jaw jerks only)	□
2	**Upper limbs:**	
	Unaffected	□
	Function affected (e.g. difficulty with keys, doorknobs, zips, bags)	□
	Affected on examination only (accepted sign: wasting of the first dorsal interossei)	□
	Affected on reflex examination only (accepted signs: the presence of pectoral reflexes or Hoffman's sign)	□

3	**Lower limbs:**	
	Unaffected	□
	Function affected e.g. difficulty walking, falls, cramps etc.	□
	Affected on examination only (accepted signs: gait stiffness or foot drop)	□
	Affected on reflex examination only (accepted signs: crossed adductor reflexes, pathologically brisk patellar reflexes or ankle clonus)	□
4	**Weight(in Kg):** an estimate is acceptable if actual weight is not known or measurable Current:_____ Baseline Weight:_____ Not documented □	
5	**RIG needed/in-situ:** Yes □ No □ Not documented □	
6	**Respiratory symptoms (exertional dyspnea, orthopnoea or excessive daytime sleepiness):** Yes □ No □ Not documented □	
7	**Respiratory function Please complete what is available:** Not documented □ • SNIP (cm H2O):_____ • Recent SNIP in last 3 months:_____ • FVC:_____ • Pulse Oximetry SpO2:_____ • pCO2_____ • NIV needed/used: Yes □ No □ Not documented □	

Does patient fulfil any of the criteria for advanced disease requiring intervention?

Not documented □

1. RIG needed/ in-situ Y □ N □
2. NIV needed/used Y □ N □
3. Weight loss more than 10% of baseline Y □ N □
4. SNIP < 40cm H_20 or a decrease > 10cm H_20 over 3 months Y □ N □
5. Patient has respiratory symptoms ANDSNIP is < 65cm H_20 (for men) or < 55cm H_20 (for women). Y □ N □
6. FVC: < 50% of predicted FVC. Y N7.Patient has respiratory symptoms ANDFVC < 80% of predicted FVC Y □ N □
7. SpO_2on oximetry is ≤94% AND either
   - pCO2 >6kPa OR Y □ N □
   - Overnight oximetry shows ≥5 dips/hours below 80% Y □ N □

Yes to any of the above= Stage 4 □

No to all of the above: How many regions (Bulbar, Upper limb, lower limb) are involved?

- ❖ One region involved= stage 1 □
- ❖ Two regions involved=stage 2 □
- ❖ Three regions involved= stage 3 □
- ❖ Not documented □

Patient's KCL Stage:_____

Abbreviations: *SNIP Sniff Nasal Inspiratory pressure, cm H2O Centimeter of water, FVC Forced Vital Capacity, SpO2 Oxygen saturation, pCO2 Partial pressure of carbon dioxide, RIG Radiologically Inserted Gastrostomy, and NIV Non Invasive Ventilation.*

NOTE :If pulse oximetry is the only measure used to test respiratory function and SpO_2 is ≤94% and pCO_2<6kPa then arrange for the patient to have overnight oximetry.

Part IV: El Escorial and Awajii criteria for diagnosis of ALS

1. Clinically definite ALS □
    - Clinical or electrophysiological evidence by the presence of LMN as well as UMN signs in the bulbar region and at least 2 spinal regions or the presence of LMN and UMN signs in 3 spinal regions.

2. Clinically probable ALS □
    - Clinical or electrophysiological evidence by LMN and UMN signs in at least 2 regions with some UMN signs necessarily rostral to (above) the LMN signs.

3. Probable ALS–Laboratory Supported □
    - Clinical signs of UMN and LMN dysfunction are found in only 1 region but electrophysiological signs of LMN loss are observed in 2 regions.

4. Clinically possible ALS □
    - Clinical or electrophysiological signs of UMN and LMN dysfunction are found in only 1 region or UMN signs are found alone in 2 regions or LMN signs are found rostral to UMN signs.

Part V: Treatment Given

a. Motor rehabilitation Yes □ No □

b. Speech therapy Yes □ No □

Riluzole use Yes □ No □