Received 30 November 2022 | Accepted 28 December 2022
DOI: http://doi.org/10.4038/sljon.v9i1.128

SLJoN

RESEARCH ARTICLE

The clinical profile of amyotrophic lateral sclerosis patients presenting to the National Hospital of Sri Lanka

Shanika Nandasiri, Nirmali Silva, Ilma Imitiaz, Padma Gunaratne, Sunethra Senanayake, Arjuna Fernando, Kishara Gooneratne

National Hospital of Sri Lanka.

Correspondence

Shanika Nandasiri

Neurology Unit
Colombo North Teaching Hospital
Sri Lanka.

E-mail: dulanjaleen@gmail.com

Abstract

Background: Amyotrophic lateral sclerosis (ALS) is a devastating neurodegenerative disease. Published data on ALS in Sri Lanka is scarce. The aim of this study was to describe the clinical profile of ALS patients presenting to the National Hospital of Sri Lanka (NHSL).

Methods: A descriptive cross-sectional study was carried out on 33 consecutive patients with "clinically definite ALS" according to revised El-Escorial and Awaji criteria, over a two year period from 2018, in two neurology units at the NHSL.

Results: The mean age was 59.7 (±12.3) years and the majority (57.6%, n=19) were males. The average duration taken for diagnosis was 15.48 (±12.4) months. The commonest first symptom was upper limb weakness, noted in 13 (39.4%), followed by lower limb weakness in 11 (33.3%). Bulbar symptoms occurred in 27.3% (n=9). According to the King's Staging System, the percentages in Stage 1, 2 and 3 were 18.2%, 39.4% and 36.4% at the time of diagnosis. There was one patient each in the most severe categories of stage 4A and 4B. None had a family history of ALS. Four were treated with riluzole. Referal for supportive care was minimal; only 45% were referred for physiotherapy, 24.2% for occupational therapy and 75% of those with bulbar symptoms for speech and language therapy. Nutritional assessments were done in 18% (n=6) and none were referred to pulmonologists. Advance directives were not discussed with any of the patients.

Conclusion: The ALS patients presenting to the NHSL had a mean age of 59.7 years with a slight male preponderance. The average duration taken for diagnosis was 15.5 months and the commonest presentation was upper limb weakness. The majority presented in King's stage 2 or 3. Only a few were treated with disease modifying agents. Multidisciplinary care and management of disease related complications were suboptimal. Discussion of advance directives with ALS patients, is yet not part of Sri Lankan practice. This emphasizes the need to enhance the standards of care to improve the quality of life of ALS patients.

KEYWORDS
Motor neurone disease, Anterior horn cell disease, Sri Lanka

BACKGROUND

Motor neurone diseases include a range of inherited and acquired neurodegenerative conditions that affect motor neurones out of which amyotrophic lateral sclerosis (ALS) is the commonest worldwide.

The global incidence of ALS is estimated to be 2.2 per 100,000, with a prevalence of 4-5 per 100,000. These figures are based on western population based studies.[1] In contrast, the incidence was shown to be 0.89 per 100,000 person years in east Asia and 0.79 per person years in south Asia.[2] The exact reason for this geographical difference is yet to be elucidated and is thought to be due to the effects of different genetic and environmental risk factors.[2]

The average age of ALS onset is in the late 5th or early 6th decades and the risk of development increases with age. It classically presents with features of mixed upper and lower motor neurone dysfunction affecting multiple body segments. The diagnosis of ALS is made based on the revised El Escorial and Awaji criteria,[1] which includes clinical and electro-physiological parameters. There are no established biomarkers to confirm the diagnosis or to predict the progression of disease.[3]

Nearly 90% of cases of ALS are sporadic, however, about 10% are considered to be familial.[1] The familial forms are commonly related to mutations in the *C9orf72* gene. The *SOD1*, *TARDBP* (associated with TDP-43 inclusions) and *FUS* (fused in sarcoma mutation) genes are seen in patients with early onset ALS; usually encountered in the second or third decade.[4]

Despite extensive research and clinical trials, there is still no cure for ALS. There are a few disease modifying medications like riluzole and edaravone with little proven efficacy.[5,6] As such, the management of ALS is mainly dependant on supportive care involving a multidisciplinary team to improve the quality of life. In fact, some of these measures like non-invasive ventilation, have been shown to improve survival.[7,8]

ALS is not an uncommon disease in neurology practice in Sri Lanka. Although many advances have taken place with regard to pharmacological and non-pharmacological management of ALS around the world, little has changed in the management of ALS in the Sri Lankan setting. There are no studies published on ALS in Sri Lanka. Demographic data, clinical pattern, prognosis as well as the genetic basis of ALS in Sri Lankan patients is yet to be elucidated.

The objective of this study was to describe the clinical profile of ALS patients presenting to the neurology service at the National Hospital, the leading tertiary care facility in Sri Lanka. It also investigated disease related complications, delays in diagnosis, adequacy of supportive care provided and their end of life decisions.

METHODS

A descriptive cross-sectional study was carried out in two neurology units at the National Hospital of Sri Lanka. A total of 33 consecutive patients with the diagnosis of "clinically definite ALS" according to the El Escorial and Awaji criteria, presenting from May 2018 to August 2020, were included in the study.

Data was gathered using an interviewer-administered questionnaire. The medical records, bed head tickets and the neurophysiological investigations (nerve conduction study/ electromyography) were reviewed to improve the accuracy of diagnosis. The symptoms of the first presentation, were categorised depending on the body region involved. A neurological examination was caried out and the presence or absence of upper motor and lower motor neurone deficits in the upper limb, lower limb and the bulbar regions were documented. The date of the confirmatory neurophysiological test was considered as the date of definitive diagnosis. The clinical severity was categorised based on the King's College ALS clinical staging system.[9] During the interview, inquiries were made for the presence of disease related complications and the clinical records were examined to confirm speciality referrals and to check for information on genetic testing.

Statistical analysis

Statistical analysis was done using SPSS version 26. Descriptive statistics were used to interpret data.

RESULTS

A total of 33 patients, presenting to the two units over the study period, with the diagnosis of clinically definite ALS were included in the study. The mean age of the participants at the time of recruitment to the study was 59.7 (SD± 12.3) years. Of the participants 57.6% (n=19) were males and the male:female ratio was 1.36:1. The majority 87.9% (n=29) were Sinhalese and the rest were Tamils. The patients' educational level was equally represented across the three categories of educational levels, below grade five level (33.3%), up to ordinary level (33.3%) and beyond ordinary level (36.4%). Of the study population, 48.5% (n=16) had co-morbid states. These were hypertension (33.3%), diabetes mellitus (18.2%), dyslipidaemia (15.2%), and ischaemic heart disease (9.1%).

The average duration taken to confirm the diagnosis was 15.48 (SD±12.4) months. The commonest first presentation was upper limb weakness, observed in 39.4% (n=13). Lower limb weakness as the first manifestation was seen in 33.3% (n=11), while the balance 27.3% (n=9) presented with bulbar symptoms. According to the King's staging system of disease severity, at the time of diagnosis, 18.2% (n=6), 39.4% (n=13) and 36.4% (n=12) were in stages 1, 2 and 3 respectively. There was one each (3%) in stage 4A and 4B. [Figure 1]

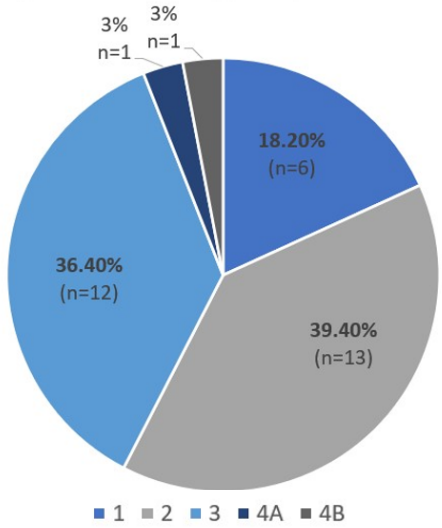

FIGURE 1 **King's clinical stage at presentation. Stage 1: involvement of one clinical region, Stage 2: involvement of a second clinical region, Stage 3: involvement of a third clinical region, Stage 4a: Nutritional failure, Stage 4b: Respiratory failure.**

None had a family history of a similar illness among first degree relatives. Genetic confirmation was available for none.

There were 4 patients who were treated with riluzole 50mg twice per day. During the clinical management 45% (n=15) and 24.2% (n=8) were referred for physiotherapy and occupational therapy respectively. There were six patients (18.2%) on treatment for depression however only two (6.1%) were referred for psychiatry assessment and three (9.1%) out of all were seen by the social service officers. A nutritional assessment was done in 18.2% (n=6). None were referred to pulmonology services. Of the 24 patients with bulbar symptoms, 75% (n=18) were referred to speech and language therapy and one had a gastrostomy tube inserted. End of life decisions were not discussed with any of the patients. A summary of these findings are given in Table 1.

TABLE 1 **Demographic features and clinical details of patients diagnosed with amyotrophic lateral sclerosis**

Characteristics		Number (n)	Percentage (%)
Gender	Male	19	57.6%
	Female	14	42.4%
Ethnicity	Sinhalese	29	87.9%
	Tamils	4	12.1%
Comorbidities	Diabetes mellitus	6	18.2%
	Hypertension	11	33.3%
	Dyslipidaemia	5	15.2%
	Ischemic heart disease	3	9.1%
	Other	8	24.2%
First symptom	Upper limb weakness	13	39.4%
	Lower limb weakness	11	33.3%
	Bulbar symptoms	9	27.3%
Adequacy of multidisciplinary care provided	Physiotherapy	15	45.5%
	Occupational therapy	8	24.2%
	Nutritional assessment	6	18.2%
	Psychiatry review	2	6.1%
	Pulmonology review	0	0.0%
	Gastroenterology review	3	9.1%
	Social service support	3	9.1%
	Assessment by speech therapist	18	54.5%

DISCUSSION

ALS is known to affect the middle-aged community, in the 5th and 6th decades, with a slight male predominance. The male preponderance is consistently observed across studies from east and west.[10,11] Findings in the present cohort from Sri Lanka also showed similar male predominance and a mean age of disease onset.

Ethnic groups in Sri Lanka include a majority of Sinhalese (75%) followed by 15.4% Sri Lankan and Indian Tamils with the rest being Moor and other minorities. In keeping with this distribution of races, this study cohort consisted of predominantly Sinhalese patients, while the rest being Tamils. There was no evidence of predilection to a particular ethnic group.

The commonest reported clinical presentation of ALS is insidious onset progressive limb weakness in about 70% and bulbar symptoms in 25%.[1] In this study, similar figures of 72.7% with limb weakness and 27.3% with bulbar symptoms were noted. Globally, primary presentation with respiratory onset is rare and is due to the lower motor neurone dysfunction of the diaphragm and accessory respiratory muscles. There were no patients presenting with respiratory muscle weakness in our study.

The average duration from symptom onset to definitive diagnosis of ALS in this cohort was 15.48 (4-48) months. This figure is consistent with prior studies which report median diagnostic times of 8-15 months.[12] There are a myriad of reasons for the delay in arriving at the definitive diagnosis of ALS. Slow progression of the disease, absence of sensory symptoms such as pain, non-availability of a biochemical test or biomarkers, shortage of expertise in the relevant field, such as the services of neurologists and neurophysiologists, are some.

The diagnosis of ALS is made based on the revised El Escorial and Awaji criteria, which includes clinical (progressive weakness with upper and lower motor signs on examination) and electrophysiological parameters. El Escorial and Awaji criteria are not a measure of disease activity that indicate the prognosis of the affected patients. Therefore, various staging systems such as the King's staging system, ALS Milano-Torino staging system (MiToS) were introduced and have gained acceptance lately.[13,14] These staging systems can be used to categorise the severity of the illness as well as for prognostication. These two scores are considered complementary. In our study group, most patients were in stage 2 and 3, according to the King's staging system at the time of diagnosis. This indicates clinical involvement of 2 or 3 motor regions. The patient in stage 4A required Percutaneous Endoscopic Gastrostomy (PEG) insertion and the patient in 4B had respiratory muscle involvement at the time of diagnosis, both indicating a worse prognosis.

Riluzole, is a disease modifying agent and the only drug currently available for ALS in Sri Lanka. It is a glutamatergic transmission inhibitor which has shown some reduction in the ALS functional rating scale. Of the four patients who were treated with riluzole 50 mg twice per day in the study group, three were in King's stage 3 and one was in stage 2. During the limited follow up, they all lived more than six months from commencement of pharmacotherapy without a major functional decline. However, the number of patients on therapy was too small to comment on the efficacy or a survival benefit.

In the absence of significantly effective definitive therapies, the management of ALS is mainly dependant on multidisciplinary non pharmacological interventions to improve the quality of life. These measures have been shown to improve survival.[7,8]

In ALS, weakness of muscles leading to physical disability that requires the attention of physiotherapists and occupational therapists, is a predominant symptom. Even though there is no strong evidence to suggest the efficacy of exercise in ALS, it is associated with a functional benefit and helps maintain the muscle mass.[15] Furthermore, patients can be provided with assistive devices that would enable them to carry out their activities of daily living and help them maintain their independence.[16] In our study, these services were offered minimally.

Respiratory muscle paralysis is the most serious complication leading to death in ALS patients. As such, it is mandatory for ALS patients to have serial respiratory function assessments starting from the time of diagnosis. Various respiratory parameters e.g., maximal sniff inspiratory force, overnight oximetry, maximal inspiratory pressure, vital capacity etc., are used to guide timely treatment. Non-invasive positive pressure ventilation is used at centres of excellence world-wide and has been shown to improve survival. [17] Pulmonology referral and review by speech and language therapists, even in those with bulbar involvement, was inadequate in our setting.

As weight loss in ALS is common and is not entirely due to dysphagia, all patients with ALS need to be assessed by nutritionists regularly even in the absence of bulbar involvement, with interventions depending on each patient's need.[18] In the reported study only a minimal number were referred for nutritional assessment.

Being diagnosed with an incurable disease with functional impairment is indeed a life changing event to the patient as well as to the family. Therefore, the threshold for depression in these patients is low.[19] Hence interventions and support should be discussed and provided, not only to the patient, but also to the caregivers whenever possible. Cognitive and behavioural problems which could be a part of ALS itself, depression, anxiety and insomnia should be dealt with appropriately.

Another important but often neglected aspect in caring for ALS patients is, effective communication.[20,21] After discussing the diagnosis and prognosis, health care providers should gradually engage patients into discussions about end of life decisions and advance directives, preferably before they lose their capacity to make decisions. Commonly anticipated issues like need for intubation, resuscitation, legal issues such as granting power of attorney etc., should be discussed with patients in the presence of the family members depending on the patients' preference. In our study, end of life decisions were not discussed with any of the patients.

Limitations of the study

The small sample size of 33 patients was a limitation to generalise the study findings. Furthermore, this being a single centre study, leads to selection bias. Poor attendance in the follow up clinics was a major drawback, limiting the assessment of symptom progression.

CONCLUSION AND RECOMMENDATIONS

This study showed that the ALS patients presenting to a tertiary care neurology service in Sri Lanka demonstrated similar demographics to those reported in other studies. The time to diagnosis was rather delayed. Although most cases presented in King's stage 2 or 3, only a very few were treated with disease modifying agents. The multidisciplinary care provided, surveillance and management of disease related complications were suboptimal. Discussing advance directives with ALS patients has still not come into Sri Lankan practice.

Improvement of supportive care services for ALS patients, introduction of effective communication practises and discussions on end of life issues are recommended. Larger studies to identify neurophysiological and clinical variations as well as the genetic landscape are suggested.

ACKNOWLEDGEMENTS

We thank all the patients and their family members for their participation in the study.

REFERENCES

1. Quinn C, Elman L. Amyotrophic Lateral Sclerosis and Other Motor Neuron Diseases. *Continuum* (Minneap Minn). 2020; 26(5):1323-47. doi:10.1212/CON.0000000000000911
2. Shahrizaila N, Sobue G, Kuwabara S et al. Amyotrophic lateral sclerosis and other motor neurone diseases in Asia. *J Neurol Neurosurg Psychiatry*. 2016;87:821-30. doi:10.1136/jnnp-2015-312751
3. Gille B, De Schaepdryver M, Dedeene L, et al. Inflammatory markers in cerebrospinal fluid: independent prognostic biomarkers in amyotrophic lateral sclerosis? *J Neurol Neurosurg Psychiatry.* 2019;90(12):1338-46. doi:10.1136/jnnp-2018-319586
4. Laaksovirta H, Peuralinna T, Schymick JC, et al. Chromosome 9p21 in amyotrophic lateral sclerosis in Finland: a genome-wide association study. *Lancet Neurol*. 2010;9(10):978-85. doi:10.1016/S1474-4422(10)70184-8.
5. Miller RG, Mitchell JD, Moore DH. (2012). Riluzole for amyotrophic lateral sclerosis (ALS)/motor neuron disease (MND). *Cochrane Database Syst Rev*. 2012;2012(3): CD001447. doi: 10.1002/14651858.CD001447.pub3.
6. Shefner J, Heiman-Patterson T, Pioro EP, et al. Long-term edaravone efficacy in amyotrophic lateral sclerosis: Post-hoc analyses of Study 19 (MCI186-19). *Muscle Nerve*. 2020;61(2): 218-21. doi: 10.1002/mus.26740.
7. Jacobs TL, Brown DL, Baek J, et al. Trial of early non-invasive ventilation for ALS: a pilot placebo-controlled study. *Neurology.* 2016;87(18):1878-83. doi:10.1212/WNL.0000000000003158.
8. Miller RG, Jackson CE, Kasarskis EJ, et al. Practice parameter update: the care of the patient with amyotrophic lateral sclerosis: drug, nutritional, and respiratory therapies (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2009;73(15): 1218-26. doi:10.1212/WNL.0b013e3181bc0141.
9. Corcia P, Beltran S, Lautrette G, Bakkouche S, Couratier P. Staging amyotrophic lateral sclerosis: A new focus on progression. *Rev Neurol (Paris)*.2019;175(5):277-82. doi:10.1016/j.neurol. 2018.09.017
10. Marin B, Logroscino G, Boumediene F, et al. Clinical and demographic factors and outcome of amyotrophic lateral sclerosis in relation to population ancestral origin. *Eur J Epidemiol* . 2016; **31**(3): 229-45. doi: 10.1007/s10654-015-0090-x.
11. McCombe PA, Henderson RD. Effects of gender in amyotrophic lateral sclerosis. *Gend Med*. 2010;7(6):557-70. doi: 10.1016/ j.genm.2010.11.010.
12. Paganoni S, Macklin EA, Lee A, et al. Diagnostic timelines and delays in diagnosing amyotrophic lateral sclerosis (ALS). *Amyotroph Lateral Scler Frontotemporal Degener.* 2014;15(5-6): 453-56. doi:10.3109/21678421.2014.903974
13. Balendra R, Khleifat AA, Fang T, et al. A standard operating procedure for King's ALS clinical staging. *Amyotroph Lateral Scler Frontotemporal Degener.* 2019;20(3-4):159-64. doi: 10.1080/21678421.2018.1556696.
14. Fang T, Al Khleifat A, Stahl DR, et al. Comparison of the King's and MiToS staging systems for ALS. *Amyotroph Lateral Scler Frontotemporal Degener.* 2017;18(3-4):227-32. doi: 10.1080/ 21678421.2016.1265565.
15. Dal Bello-Haas V, Florence JM. Therapeutic exercise for people with amyotrophic lateral sclerosis or motor neuron disease. *Cochrane Database Syst Rev.* 2013;2013(5):CD005229. doi: 10.1002/14651858.CD005229.pub3.
16. Peseschkian T, Cordts I, Gunther R, et al. A Nation-Wide, Multi-Center Study on the Quality of Life of ALS Patients in Germany. *Brain Sci*. 2021;11(3):372. doi: 10.3390/brainsci11030372.

17. Fitting JW, Paillex R, Hirt L, Aebischer P, Schluep M. Sniff nasal pressure: a sensitive respiratory test to assess progression of amyotrophic lateral sclerosis. *Ann Neurol.* 1999;46(6): 887-93.

18. Borasio GD, Voltz R, Miller RG. Palliative care in amyotrophic lateral sclerosis. *Neurol Clin.* 2001;19(4):829-47. doi:10.1016/s0733-8619(05)70049-9

19. Heidari ME, Nadali J, Parouhan A, et al. Prevalence of depression among amyotrophic lateral sclerosis (ALS) patients: A systematic review and meta-analysis. *J Affect Disord*. 2021;287:182-90. doi:10.1016/j.jad.2021.03.015

20. Miller RG, Rosenberg JA, Gelinas DF, et al. Practice parameter: the care of the patient with amyotrophic lateral sclerosis (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology: ALS Practice Parameters Task Force. *Neurology.* 1999;52(7):1311-23. doi:10.1212/wnl.52.7.1311

21. Andersen PM, Abrahams S, et al. EFNS Task Force on Diagnosis and Management of Amyotrophic Lateral Sclerosis. EFNS guidelines on the clinical management of amyotrophic lateral sclerosis (MALS) – revised report of an EFNS task force. *Eur J Neurol*. 2012;19(3):360-75. doi: 10.1111/j.1468-1331.2011.03501.x.