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Evaluation of quality of life and mood disorders in caregivers of patients with amyotrophic lateral sclerosis: A single-center cross-sectional study

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Keywords
Amyotrophic Lateral Sclerosis; Caregiver; Anxiety; Depression; Quality of Life

Abstract

Background: Caregivers of patients with amyotrophic lateral sclerosis (ALS) may suffer from anxiety, depression, and reduced quality of life (QoL). Our goal was to evaluate the QoL and mood disorders in caregivers and their correlation with the patients' demographic, physical, and mental conditions.

Methods: We analyzed data from 39 patients with ALS and their caregivers. Patients completed questionnaires of anxiety assessed by Generalised Anxiety Disorder Assessment (GAD-7), depression using the Beck Depression Inventory-II (BDI-II), and QoL via 40-item Amyotrophic Lateral Sclerosis Assessment Questionnaire (ALSAQ-40). Physical impairment was also measured in the patients using the revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R). Caregivers were also assessed by BDI-II, GAD-7, and 36-item Short-Form Health Survey questionnaire (SF-36).

Results: The prevalence of depression and anxiety in the patients was 82.1% and 71.8%, respectively. Caregivers also had higher rates of anxiety and depression and lower levels of QoL in comparison with the general population (anxiety: 66.7%, depression: 43.6%). Depression and anxiety were considerably associated with worsened QoL in the caregivers. None of the demographic, physical, or mental characteristics of patients with ALS were related to either mood status

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or QoL of the caregiver population.
Conclusion: Caregivers experience higher rates of anxiety and depression and lower QoL in comparison with the general population. The severity of mood disorders is inversely associated with the physical and mental domains of caregivers' QoL. Nonetheless, QoL in the caregivers is not affected by the physical or mental disability of the patients.

Introduction

Amyotrophic lateral sclerosis (ALS) is a rapidly progressive neurodegenerative disease characterized by the involvement of upper and lower motor neurons leading to weakness and disability of the skeletal muscles as well as the inability to speak normally or swallow, respiratory problems, and eventually death.[1,2] Despite extensive researches, curative therapy for ALS has not been known until today; hence, palliative care should be considered with the aim of reducing the symptoms of the disease and increasing the quality of life (QoL).[1] Patients and caregivers may suffer from anxiety and depression during ALS disease, influencing their QoL.[3,4]

Caregivers of patients usually endure a significant burden as the symptoms progress in their patients. Patients with ALS need assistance with all of their daily living activities since their ability to speak or write is impaired. Physical demands for appropriate care become more severe by the progression of the disease. It is estimated that ALS caregivers spend 11 hours a day with the patient and feel a profound responsibility for their patients.[5] Findings are controversial regarding the correlation between the mood status of the patients and their caregivers;[5] some studies indicated that anxiety and depression in caregivers had a relation with physical and mental disability in patients while other studies did not find such an association.[5-7] Since caregivers' wellbeing may have an impact on the psychological and physical status of patients, attention to the caregiver's mental health can help patient distress.[6,8]

Considering the inconsistent results regarding mood disorders and QoL in ALS caregivers and their contributing etiologies, as well as the fact that such a study in Persian patients with ALS was lacking, we intended to study the QoL as well as depression, anxiety, and physical status and their interactions in both patients and caregivers.

Materials and Methods

Settings: In this cross-sectional study, we enrolled 39 patients with ALS and their caregivers in ALS Clinic of Shariati Hospital, affiliated to Tehran University of Medical Sciences, Tehran, Iran, from March 2018 to October 2019. Written informed consent was obtained from patients and their caregivers following the description of their ability to withdraw from the study without any adverse effect on their healthcare. The protocol of the study was in accordance with the latest versions of the Declaration of Helsinki[9] and was approved by the Ethical Committee of Tehran University of Medical Sciences (IR.TUMS.MEDICINE.REC.1397.685).

Participants: Eligible participants were patients who met the criteria for definite or probable ALS diagnosis according to the revised El Escorial criteria,[10] as well as their caregivers. A caregiver was defined as a person who lives with the patient and who provides the patient with the most care and assistance.[6] The exclusion criteria for both patients and caregivers were: inability to complete the questionnaires, Mini-Mental State Examination (MMSE) score ≤ 24, paid caregivers, and history of fatal diseases such as malignancy.

Demographic information was collected, including age, gender, and education, along with clinical data, including disease duration and disease onset (bulbar onset or limb onset). The 40-item Amyotrophic Lateral Sclerosis Assessment Questionnaire (ALSAQ-40) and 36-item Short-Form Health Survey questionnaire (SF-36) were used to evaluate the QoL of patients with ALS and their caregivers, respectively. The Beck Depression Inventory-II (BDI-II) and the Generalized Anxiety Disorder Assessment (GAD-7) were employed to quantify depression and anxiety in patients and caregivers. Patients' physical function was assessed by the revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R).

Questionnaires: ALSAQ-40 consists of 5 subscales, including physical mobility, daily living activities and independence, eating and drinking, communicational abilities, and emotional reactions. The score of items ranges from 0, representing a high level of QoL, to 100, representing a low level of QoL. The ALSAQ-40 was previously translated and validated in the Persian language.[11]

The SF-36 questionnaire is a self-administered measure that combines eight general health subscales: physical function, physical role function, bodily pain, general health, vitality, social function, emotional function, and mental health. Besides, the eight items are summarized into two main domains: physical health dimension (PHD) and mental health dimension (MHD). All scores were interpreted

with a 0-100 score, where higher scores represent better QoL (in contrast to ALSAQ-40). The questionnaire had been previously standardized in the Iranian population.[12]

BDI-II is a self-reporting questionnaire consisting of 21 questions that provide a total score between 0 to 63, in which scores of 0-13, 14-19, 20-28, and 29-63 represent normal, mild, moderate, and severe depression, respectively.[13] We used the Persian validated version of questionnaire.[14]

GAD-7 is a 7-item scale with total score ranging from 0 to 21, while the cutpoints for mild, moderate, and severe symptoms are 5, 10, and 15, respectively.[15]

The ALSFRS-R includes 12 questions that measure upper extremity, lower extremity, and bulbar functions, and respiration. The score varies between 0 (maximum impairment) and 48 (normal function).[16]

We used SPSS software (version 24, IBM Corporation, Armonk, NY, USA) to analyze the data. The Shapiro-Wilk test and probability graphs were used to check for the normal distribution of the data. For the correlations between QoL domains (physical and mental domains) and other scales, when the distribution was normal, we used the Pearson correlation test. In case of non-normal distribution, we used the Spearman correlation test. Variables with normal distribution were presented as mean ± standard deviation (SD) while the data with abnormal distribution were presented as median [interquartile range (IQR), 25^{th}-75^{th} percentile]. The P-values < 0.05 were regarded significant.

Results

Demographic characteristics: In this study, 39 patients and 39 caregivers were enrolled. The mean age was 57.7 ± 8.8 for the patients and 43.3 ± 13.8 for the caregivers. From 39 patients and caregivers, 18 patients (46.2%) and 19 caregivers (48.7%) were women. The ALSFRS-R score in patients was 27.9 ± 10.0 and the average disease duration was 4.0 ± 2.9 years. Other demographic and descriptive features of the caregivers and patients are summarized in table 1. In the caregivers, the PHD score of SF-36 was 52.6 ± 11.0 and 36.6 ± 12.4 for the MHD (Table 1). For the patients, the highest (worst) score was for physical mobility (70.2 ± 33.3) and the least was for emotional aspects (50.6 ± 24.8) (Table 1).

Mood disorders: In the general Iranian population, the prevalence of depression using BDI was estimated at 37.3% based on a recent meta-analysis; and in a large cohort, the prevalence of anxiety was 15.6%.[17,18] In our study, the prevalence of depression and anxiety in the patients was 82.1% and 71.8%, respectively, which were both considered higher than the prevalence of mentioned mood disorders in the general population [odds ratio (OR) for depression = 2.2, P < 0.001; OR for anxiety = 4.72, P < 0.001]. In the caregivers, the prevalence of depression and anxiety was 43.6% and 66.7%, respectively, both higher than that in the general Iranian population;[17] however, the prevalence of depression was not significantly different in comparison with the general population (OR for depression = 1.17, P = 0.270; OR for anxiety = 4.39, P < 0.001).

The patients compared to the caregivers demonstrated significantly higher BDI score (19.8 ± 9.0 vs. 13.6 ± 8.3, t = 3.18, P = 0.001), whereas GAD-7 score was not significantly different between two groups (8.7 ± 5.8 vs. 7.7 ± 4.8, t = 0.85, P = 0.200).

QoL in caregivers: Concerning the relationship between mood disorders and QoL in caregivers, a significant correlation was found between BDI score and PHD (r = -0.38, P = 0.020) as well as MHD (r = -0.50, P < 0.001). In terms of anxiety, the correlation between GAD-7 score and PHD was not significant (r = -0.29, P = 0.080) whereas the correlation between GAD-7 score and MHD was significant (r = -0.51, P < 0.001).

Our results showed that older age of caregivers was correlated with lower PHD in caregivers (r = -0.47, P < 0.010); however, no significant correlation with MHD was detected (r = -0.13, P = 0.420).

Considering gender in caregivers, we found no significant difference of PHD and MHD between two genders [PHD (women): 49.5 ± 11.7, PHD (men): 55.6 ± 9.6, P = 0.080; MHD (women): 33.4 ± 12.7, MHD (men): 39.6 ± 11.6, P = 0.120].

The association between patients' factors and QoL and mood status of caregivers: None of the demographic and clinical features in subjects with ALS were related to mood status or QoL of their caregivers (P > 0.05) (Table 2). Neither the scores of mood disorders (BDI and GAD-7) nor those of QoL (ALSAQ-40 subscales) in the patients were associated with SF-36 subdomains in the caregivers (P > 0.050) (Table 2).

Discussion

In this study, we sought to describe the status of QoL and mood in caregivers of patients with ALS. The results showed a higher prevalence of depression and anxiety in patients and their caregivers than the general population.

Table 1. Demographic and descriptive features of the patients and caregivers

Variables			Patients (n = 39)	Caregivers (n = 39)
Age (year) (mean ± SD)			57.7 ± 8.8	43.3 ± 13.8
Gender (F/M)			18/21	19/20
ALSFRS-R (mean ± SD)			27.9 ± 10.0	-
Duration (year) (mean ± SD)			4.0 ± 2.9	-
Disease onset (limb/bulbar)			23/16	-
Education [n (%)]		Not educated	6 (15.4)	0 (0)
		Less than diploma	4 (10.3)	7 (17.9)
		Diploma	25 (64.1)	18 (46.2)
		University degree	4 (10.3)	14 (35.9)
Depression [n (%)]		Minimal	7 (17.9)	22 (56.4)
		Mild	13 (33.3)	7 (17.9)
		Moderate	14 (35.9)	8 (20.5)
		Severe	5 (12.8)	2 (5.1)
Anxiety [n (%)]		No	11 (28.2)	13 (33.3)
		Mild	11 (28.2)	12 (30.8)
		Moderate	8 (20.5)	11 (28.2)
		Severe	9 (23.1)	3 (7.7)
ALSAQ-40 subdomains (mean ± SD)		Physical mobility	70.2 ± 33.3	-
		Activities of daily living	63.0 ± 29.3	-
		Eating and drinking	53.8 ± 26.6	-
		Communication	53.7 ± 36.3	-
		Emotional aspect	50.6 ± 24.8	-
SF-36 (mean ± SD)	Subdomains	Vitality	-	48.0 ± 8.9
		Physical functioning	-	49.7 ± 9.6
		Bodily pain	-	50.7 ± 11.0
		General health perceptions	-	47.6 ± 8.8
		Physical role functioning	-	45.0 ± 13.7
		Emotional role functioning	-	34.7 ± 18.7
		Social role functioning	-	39.9 ± 9.8
		Mental health	-	41.2 ± 8.7
	Dimensions	Physical health	-	52.6 ± 11.0
		Mental health	-	36.6 ± 12.4

ALSFRS-R: Revised Amyotrophic Lateral Sclerosis Functional Rating Scale; ALSAQ-40: 40-item Amyotrophic Lateral Sclerosis Assessment Questionnaire; SF-36: 36-item Short-Form Health Survey; SD: Standard deviation

Besides, in the caregivers, the severity of mood disorders was negatively associated with the physical and mental aspects of QoL. In contrast, none of the demographic, clinical, or mood characteristics of patients with ALS influenced mood status and QoL of the caregiver population.

It has been well established that caregivers of patients with terminal or progressive diseases usually experience high levels of distress. For instance, several studies have shown significant mood problems among caregivers of patients with dementia,[19,20] cancer,[21] multiple sclerosis (MS),[22] acquired immunodeficiency syndrome (AIDS),[23] Parkinson's disease (PD),[24] and brain injury.[25] Caregivers of patients with ALS also deal with emotional, social, and even physical problems and, therefore, are susceptible to various mood disorders.[6] However, in the results obtained from previous studies, there is controversy about whether the prevalence of depression and anxiety in caregivers differs from either patients with ALS or healthy controls.[3,26,27]

In the present study, the prevalence of depression and anxiety in patients with ALS was much higher than previous studies conducted in other countries,[3,28-30] which may stem from variable supportive care in different countries, different cultural and demographic features, religion, willingness to express personal feelings and beliefs to medical personnel, different medications, or using different scales for the assessment.[31] Regarding the rate of mood disorders in the caregivers, we identified that it was higher than the general population but lower than the patients.

Meanwhile, we did not find an association between depression and anxiety in caregivers' and patients' physical or psychological status. In agreement, several previous studies showed no significant association between physical and mental disability of the patients and caregivers' mental condition.[3,5,7,32]

Table 2. The association between patients' factors and mood status and quality of life (QoL) of caregivers

				Caregivers			
				BDI	**GAD-7**	**PHD**	**MHD**
Patients	Demographic and clinical factors	ALS type (mean ± SD)	Bulbar	6.4 ± 4.0	12.4 ± 6.6	52.9 ± 13.3	37.4 ± 12.4
			Limb	14.3 ± 9.3	8.5 ± 5.2	52.4 ± 9.3	36.0 ± 12.7
			P	0.20	0.49	0.89	0.74
		ALSFRS-R (r)		0.25	0.24	-0.02	-0.04
		P		0.12	0.14	0.89	0.82
		Age of patients (r)		0.16	0.25	0.12	0.19
		P		0.33	0.13	0.48	0.25
		Disease duration (r)		0.27	0.24	-0.21	-0.10
		P		0.10	0.14	0.20	0.56
	Mood	BDI (r)		0.02	0.02	0.16	-0.22
		P		0.92	0.90	0.33	0.19
		GAD-7 (r)		0.04	0	0.23	-0.09
		P		0.80	0.98	0.15	0.58
	ALSAQ-40	Physical mobility		-0.09	-0.22	-0.01	0.14
		P		0.60	0.17	0.98	0.38
		Activities of daily living		-0.19	-0.28	-0.01	0.12
		P		0.23	0.08	0.98	0.46
		Eating and drinking		-0.15	-0.11	0.04	-0.05
		P		0.37	0.52	0.80	0.76
		Communication		-0.06	0.02	-0.05	-0.06
		P		0.71	0.93	0.77	0.72
		Emotional aspect		-0.15	-0.02	0.36	-0.15
		P		0.36	0.92	0.07	0.37

ALS: Amyotrophic lateral sclerosis; ALSFRS-R: Revised Amyotrophic Lateral Sclerosis Functional Rating Scale; ALSAQ-40: 40-item Amyotrophic Lateral Sclerosis Assessment Questionnaire; BDI: Beck Depression Inventory; GAD-7: Generalised Anxiety Disorder Assessment; PHD: Physical health dimension; MHD: Mental health dimension; SD: Standard deviation

Although the existing mood burden on caregivers might not exert considerable change in the disease course of the patients, according to our findings, it is associated with worse physical functioning and mental health of the caregivers. Hence, the health team must notice and treat the psychological aspects of the illness both for patients and caregivers; even though there is no curative treatment for a progressive disease like ALS, treating depression and anxiety could enhance the QoL in both groups.

Beyond the emotional distress among caregivers, the physical strain has been of great importance, especially during the advanced stages of the disease. Caregiving to patients with ALS generally takes a considerable physical effort as they might need the help of their caregivers for ordinary movements.[6] In this regard, the physical problems of caregivers could negatively affect their QoL and could result in mood abnormalities. In support, it has been observed that older caregivers represent age-related physical difficulties and subsequently reduced QoL.[6] Here, we found that the older age of caregivers was related to lowering the physical but not mental aspect of QoL.

Our study has several limitations. First, this study contains a relatively small sample size, which may be inevitable due to the low prevalence of ALS disease. Second, we assigned patients and their caregivers from one particular ALS clinic, while mood disorders and QoL may differ in the different centers due to geographic, ethnic, or religious differences. Multi-center studies of patients with ALS from different countries could improve the generalizability of the findings. Third, different types of measurement tools for the assessment of QoL were administered to patients and caregivers, which might have affected the results. Forth, the BDI might report several patients with ALS as "depressed" false positively since it contains questions that are related to physical function. Finally, longitudinal evaluation of mood disorders and QoL in both patients and caregivers could provide more reliable information since ALS is considered a progressive neurodegenerative condition.

Conclusion

Caregivers of Iranian patients with ALS experience

higher rates of anxiety and depression and lower QoL in comparison with the general population. The severity of mood disorders, including depression and anxiety, is inversely associated with the physical and mental domains of caregivers' QoL. Nonetheless, QoL in the caregivers is not affected by the physical or mental disability of the patients. Further investigations are required to elucidate the exact features that induce physical and emotional burden in caregivers of patients with ALS.

Conflict of Interests

The authors declare no conflict of interest in this study.

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References

1. Korner S, Kollewe K, Abdulla S, Zapf A, Dengler R, Petri S. Interaction of physical function, quality of life and depression in Amyotrophic lateral sclerosis: Characterization of a large patient cohort. BMC Neurol 2015; 15: 84.
2. Jakobsson Larsson B, Ozanne AG, Nordin K, Nygren I. A prospective study of quality of life in amyotrophic lateral sclerosis patients. Acta Neurol Scand 2017; 136(6): 631-8.
3. Chen D, Guo X, Zheng Z, Wei Q, Song W, Cao B, et al. Depression and anxiety in amyotrophic lateral sclerosis: Correlations between the distress of patients and caregivers. Muscle Nerve 2015; 51(3): 353-7.
4. Kurt A, Nijboer F, Matuz T, Kubler A. Depression and anxiety in individuals with amyotrophic lateral sclerosis: Epidemiology and management. CNS Drugs 2007; 21(4): 279-91.
5. Rabkin JG, Albert SM, Rowland LP, Mitsumoto H. How common is depression among ALS caregivers? A longitudinal study. Amyotroph Lateral Scler 2009; 10(5-6): 448-55.
6. Pagnini F, Rossi G, Lunetta C, Banfi P, Castelnuovo G, Corbo M, et al. Burden, depression, and anxiety in caregivers of people with amyotrophic lateral sclerosis. Psychol Health Med 2010; 15(6): 685-93.
7. Olsson Ozanne AG, Strang S, Persson LI. Quality of life, anxiety and depression in ALS patients and their next of kin. J Clin Nurs 2011; 20(1-2): 283-91.
8. Chio A, Gauthier A, Calvo A, Ghiglione P, Mutani R. Caregiver burden and patients' perception of being a burden in ALS. Neurology 2005; 64(10): 1780-2.
9. World Medical Association. World medical association declaration of Helsinki: Ethical principles for medical research involving human subjects. JAMA 2013; 310(20): 2191-4.
10. Brooks BR, Miller RG, Swash M, Munsat TL. El Escorial revisited: Revised criteria for the diagnosis of amyotrophic lateral sclerosis. Amyotroph Lateral Scler Other Motor Neuron Disord 2000; 1(5): 293-9.
11. Shamshiri H, Eshraghian MR, Ameli N, Nafissi S. Validation of the Persian version of the 40-item amyotrophic lateral sclerosis assessment questionnaire. Iran J Neurol 2013; 12(3): 102-5.
12. Montazeri A, Goshtasebi A, Vahdaninia M, Gandek B. The Short Form Health Survey (SF-36): Translation and validation study of the Iranian version. Qual Life Res 2005; 14(3): 875-82.
13. Ghassemzadeh H, Mojtabai R, Karamghadiri N, Ebrahimkhani N. Psychometric properties of a Persian-language version of the Beck Depression Inventory-Second edition: BDI-II-PERSIAN. Depress Anxiety 2005; 21(4): 185-92.
14. Beck AT, Steer RA, Brown GK. BDI-II, beck depression inventory: Manual. New York, NY: Psychological Corporation; 1996.
15. Naeinian MR, Shairi MR, Sharifi M, Hadian M. To study reliability and validity for a brief measure for assessing generalized anxiety disorder (GAD-7). Clinical Psychology & Personality 2011; 3(4): 41-50. [In Persian].
16. Cedarbaum JM, Stambler N, Malta E, Fuller C, Hilt D, Thurmond B, et al. The ALSFRS-R: A revised ALS functional rating scale that incorporates assessments of respiratory function. BDNF ALS Study Group (Phase III). J Neurol Sci 1999; 169(1-2): 13-21.
17. Mohamadi M, Mohaqeqi Kamal SH, Vameghi M, Rafey H, Setareh Forouzan A, Sajjadi H. A meta-analysis of studies related prevalence of depression in Iran. J Research Health 2017; 7(1): 581--93.
18. Hajebi A, Motevalian SA, Rahimi-Movaghar A, Sharifi V, Amin-Esmaeili M, Radgoodarzi R, et al. Major anxiety disorders in Iran: Prevalence, sociodemographic correlates and service utilization. BMC Psychiatry 2018; 18(1): 261.
19. Mittelman MS, Ferris SH, Shulman E, Steinberg G, Ambinder A, Mackell JA, et al. A comprehensive support program: Effect on depression in spouse-caregivers of AD patients. Gerontologist 1995; 35(6): 792-802.
20. Schulz R, O'Brien AT, Bookwala J, Fleissner K. Psychiatric and physical morbidity effects of dementia caregiving: Prevalence, correlates, and causes. Gerontologist 1995; 35(6): 771-91.
21. Harding R, Higginson IJ, Donaldson N. The relationship between patient characteristics and carer psychological status in home palliative cancer care. Support Care Cancer 2003; 11(10): 638-43.
22. Peters M, Jenkinson C, Doll H, Playford ED, Fitzpatrick R. Carer quality of life and experiences of health services: A cross-sectional survey across three neurological conditions. Health Qual Life Outcomes 2013; 11: 103.
23. Folkman S, Chesney MA, Cooke M, Boccellari A, Collette L. Caregiver burden in HIV-positive and HIV-negative partners of men with AIDS. J Consult Clin Psychol 1994; 62(4): 746-56.
24. Cifu DX, Carne W, Brown R, Pegg P, Ong J, Qutubuddin A, et al. Caregiver distress in parkinsonism. J Rehabil Res Dev 2006; 43(4): 499-508.
25. Gillen R, Tennen H, Affleck G, Steinpreis R. Distress, depressive symptoms, and depressive disorder among caregivers of patients with brain injury. J Head Trauma Rehabil 1998; 13(3): 31-43.
26. Lillo P, Mioshi E, Hodges JR. Caregiver burden in amyotrophic lateral sclerosis is more dependent on patients' behavioral changes than physical disability: A comparative study. BMC Neurol 2012; 12: 156.
27. Miyashita M, Narita Y, Sakamoto A, Kawada N, Akiyama M, Kayama M, et al. Care burden and depression in caregivers caring for patients with intractable neurological diseases at home in Japan. J Neurol Sci 2009; 276(1-2): 148-52.
28. Rabkin JG, Albert SM, Del Bene ML, O'Sullivan I, Tider T, Rowland LP, et al. Prevalence of depressive disorders and change over time in late-stage ALS. Neurology 2005; 65(1): 62-7.
29. Gauthier A, Vignola A, Calvo A, Cavallo E, Moglia C, Sellitti L, et al. A longitudinal study on quality of life and depression in ALS patient-caregiver couples. Neurology 2007; 68(12): 923-6.
30. Ferentinos P, Paparrigopoulos T, Rentzos M, Zouvelou V, Alexakis T, Evdokimidis I. Prevalence of major depression in ALS: Comparison of a semi-structured interview and four self-report measures. Amyotroph Lateral Scler 2011; 12(4): 297-302.
31. Taylor L, Wicks P, Leigh PN, Goldstein LH. Prevalence of depression in amyotrophic lateral sclerosis and other motor disorders. Eur J Neurol 2010; 17(8): 1047-53.
32. Grabler MR, Weyen U, Juckel G, Tegenthoff M, Mavrogiorgou-Juckel P. Death anxiety and depression in amyotrophic lateral sclerosis patients and their primary caregivers. Front Neurol 2018; 9: 1035.