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The prevalence and impacts of psychological disorders in caregivers of Chinese ALS patients

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Abstract

Objective: To investigate the prevalence and influential factors of depression, anxiety, suicidal tendency and sleep disorders in caregivers of Chinese amyotrophic lateral sclerosis (ALS) patients. *Methods:* A total of 153 ALS caregivers were investigated using the Patient Health Questionnaire-9 (PHQ-9), Self-Rating Anxiety Scale (SAS), Self-Rating Depression Scale (SDS), the Nurses' Global Assessment of Suicide Risk scale (NGASR) and Pittsburgh sleep quality index (PSQI). The risk factors related to psychological disorders in Chinese ALS caregivers were analyzed. *Results:* The medians (range) of PHQ-9, SAS, SDS, PSQI were 12 (0-27), 43 (25-80). 55.20% (25.10%-82.11%), 9 (1-21), respectively. A total of 40 (26.14%), 37 (24.18%) and 22 (14.38%) showed moderate, high and extremely high risk of suicide evaluated by NGASR. There was a negative correlation between disease duration of ALS patients and PHQ-9, SAS, SDS, NGASR, PSQI of their caregivers ($p<0.05$). Onset age of ALS was negatively related to PHQ-9 ($p<0.001$) and SDS ($p=0.003$) in ALS caregivers. Bulbar involvement was significantly related to high level of SDS in caregivers ($p=0.028$). Pet raising and regular reading was significantly associated with low PHQ-9, SDS, NGASR and PSQI ($p<0.05$). Participation in ALS-related social activities was negatively related to NGASR of ALS caregivers ($p<0.001$).
Conclusion: Depression, anxiety, poor sleep quality and risk of suicide were commonly reported by ALS caregivers. Early onset, bulbar involvement and rapid progression might exacerbate the psychological distress of ALS caregivers. Regular reading, pet raising and participation in social activities could decrease risk of suicide and improve sleep quality of ALS caregivers.

Keywords: Amyotrophic lateral sclerosis, caregivers, depression, anxiety, sleep

INTRODUCTION

Amyotrophic lateral sclerosis (ALS), also known as typical motor neuron disease (MND), is a fatal neurodegenerative disease involving both upper motor neuron (UMN) and lower motor neuron (LMN).[1] Relentless progression of limb weakness and atrophy and bulbar dysfunction result in gradual decline of function status[2], making care of others essential for ALS population. As no causative therapies have been developed to date, long-term care and symptomatic treatment has been the hallmark of ALS systematic management, which received increasing attention.[3]

Psychological distress in ALS population have been well investigated and discussed in the literature, which might have negative effects on the quality of life (QOL) of these patients.[4,5] This fatal condition puts a significant burden not only on the affected patient but also on her/his families and caregivers.[6] Close association, heavy care burden and persistent deterioration of disease condition can cause drastic impact in daily lives of ALS caregivers[7], and epidemiological investigations revealed that they might suffer from the psychological disorders as common as ALS patients, among which high prevalence of depression and anxiety is the most concerned.[8,9] We notice that only a few[8,10] studies targeted on the psychological status of Chinese ALS caregivers, which are neglected by clinicians and social workers to a large extent in China.

Therefore, we conducted a cross-sectional study to reveal the prevalence of depression, anxiety, suicidal tendency and sleep disorders in caregivers of Chinese ALS patients. Potential risk factors and impacts of these mood and sleep symptoms would also be discussed.

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METHODS

Subjects

A prospective single-center cohort study was conducted at the Department of Neurology, Peking Union Medical College Hospital (PUMCH). Patient diagnosed with ALS according to the Awaji criteria[11] was consecutively recruited and registered. All enrolled patients were recorded with their name, gender, age and clinical symptoms with detailed physical examination. All included patients were assessed using the ALS Functional Rating Scale-Revised (ALSFRS-R).[12] The maximum of ALSFRS-R score was 48. Muscle strength was measured using the Medical Research Council (MRC) score, including bilateral assessment of the following limb muscle actions: shoulder abduction, elbow flexion, elbow extension, wrist flexion, wrist extension, finger flexion, finger extension, thumb abduction, little finger abduction, hip flexion, knee flexion, knee extension, ankle dorsal extension, ankle plantar flexion, toe dorsal extension, and toe plantar flexion. The total MRC score was 160.

For the convenience of follow-up, we established an online medical platform enabling the contacts between clinicians and ALS patients or their caregivers. All enrolled patients or their caregivers could apply and consult medical issues in the platform. A follow-up interview was performed every three months either by online survey or phone call to collect a follow-up ALSFRS-R score. The progression rate was calculated by the difference of the ALSFRS-R score at the first and last visit divided by the time interval between these two visits in months (decrease of ALSFRS-R per month).[12] As of February 2024, a total of 836 patients or their caregivers could be contacted on the platform, among which 532 ones were ALS caregivers. This study was approved by the Ethics Committee of the PUMCH (JS1218). All enrolled patients provided written, informed consent to be included in the study. An online survey on psychological disorders.

We designed a online questionnaire to investigate the levels of depression and anxiety, risk of suicide, sleep quality in ALS caregivers. The questionnaire included:

(1) Demographic information (the patient's name, age, gender, nationality, the caregivers' age, gender, nationality);
(2) Onset age, disease duration and involved body regions of ALS patients;
(3) Nutritional status of ALS patients including body mass index (BMI) and food intake;
(4) ALSFRS-R scale of ALS patients[12];
(5) Treatment of ALS patients;
(6) Self-financial status; financial support and affordability for treatment. The level of financial support included personal income, support from families and relatives and support from social charity organizations and government funding. The participant was asked to rate each item from 0 to 10 points.
(7) Daily lifestyles of ALS caregivers including smoking, drinking, pet raising, occupation, reading, participation in social activities that were related to ALS;
(8) The Patient Health Questionnaire-9 (PHQ-9)[13] and Self-Rating Depression Scale (SDS)[14] for the assessment of the level of depression;
(9) Self-Rating Anxiety Scale (SAS)[15] for the assessment of the level of anxiety;
(10) The Nurses' Global Assessment of Suicide Risk scale (NGASR)[16] for the assessment of the risk of suicide;
(11) Pittsburgh sleep quality index (PSQI)[17] for the assessment of sleep quality.

The definition and relevant explanations of involved variables were provided in Supplementary Table 1. All included scales could be used in self-report surveys. The questionnaire was sent to all ALS caregivers on the contact platform and it was totally voluntary survey to avoid causing psychological trauma or emotional distress for the participants.

Statistical analysis

The Shapiro-Wilk test was used to assess whether data exhibited a normal distribution. Normally distributed variables were expressed as means (standard deviation, SD) and abnormally distributed variables were expressed as median (range). Due to the abnormal distribution, Mann-Whitney U test or Spearman coefficient was used for the analysis on the relationships between included variables. Two-sided P-values were calculated for all analyses. A value of $P < 0.05$ was considered statistically significant. Statistical analyses were performed using SPSS 23.0.

Supplementary Table 1. Definitions and explanations of involved variables

Variables	References	Option/ Score	Definition
Self financial status	The 2023 national per capita disposable income level released by the National Bureau of Statistics)	1	<5000 yuan/month
		2	5000-20000 yuan/month
		3	20000 yuan/month
Affordability for treatment		1	Giving up treatment due to the inability to afford the cost of treatment
		2	Costs of treatment significantly influence family lives
		3	Affordability of treatment with decrease of quality of life
		4	No financial burden caused by the treatment
Food intake	Comparisons with food intake before ALS onset	1	Normal
		2	Decrease of less than 1/2
		3	Decrease of more than 1/2
Educational level		1	Illiteracy
		2	Primary school
		3	Junior middle school
		4	Senior high school
		5	University/College
		6	Post graduate or above
Smoking		1	Current smoking
		2	Past smoking (quitting smoking for more than 6 months)
		3	No smoking (never smoking)
Drinking		1	Current drinking
		2	Past drinking (quitting drinking for more than 6 months)
		3	No drinking (never drinking)
PHQ-9		0-4	No depression
		5-9	Mild depression
		10-14	Moderate depression
		15-19	Over Moderate depression
		20-27	Severe depression
SAS (Standard score)		<50	No anxiety
		50-59	Mild anxiety
		60-69	Moderate anxiety
		≥70	Severe anxiety
SDS (Disease index)		<50%	No depression
		50%-59%	Mild depression
		60%-69%	Moderate depression
		≥70%	Severe depression
NGASR		≤5	Low risk of suicide
		6-8	Moderate risk of suicide
		9-11	High risk of suicide
		≥12	Extremely high risk of suicide
PSQI		≤5	Very good sleep quality
		6-10	Good sleep quality
		11-15	General sleep quality
		≥16	Poor sleep quality

Abbreviations: ALS amyotrophic lateral sclerosis; NGASR the Nurses' Global Assessment of Suicide Risk scale; PHQ-9 the Patient Health Questionnaire-9; PSQI Pittsburgh sleep quality index; SAS Self-Rating Anxiety Scale; SDS Self-Rating Depression Scale.

RESULTS

Baseline and follow-up information

We ultimately received 206 questionnaires, of which 153 (74.27%) ones were valid and included in our analysis. The other 53 ones were excluded due to lack of important information including the patient's name or missing items in several scales. The demographic characteristics of involved ALS caregivers and relevant ALS patients were presented in Table 1. Among the caregivers, 98 (64.05%) were spouses, 43 (28.10%) were the children, 7 (4.58%) were sisters, and 5 (3.27%) were brothers of the patients.

Prevalence of psychological disorders

The results of psychological scales in ALS caregivers were presented in Table 2. The medians (range) of PHQ-9 and SDS were 12 (0-27) and 55.20% (25.10%-82.11%). There were 123 (80.39%) and 97 (63.40%) that were diagnosed as anxiety when evaluated by PHQ-9 and SDS, respectively. Patients that were classified as mild, moderate, moderate to severe, severe depression in PHQ-9 were 31 (20.26%), 37 (24.18%), 17 (11.11%), 38 (24.84%) and as mild, moderate, severe depression in SDS were 41 (26.80%), 33 (21.57%), 23 (15.03%), respectively. The median (range) of SAS was 43 (25-80). There were 89 (58.17%) that were not diagnosed with anxiety, the other 23 (15.03%), 34 (22.22%) and 7 (4.58%) were classified as mild, moderate, high levels of anxiety in SAS, respectively. A total of 40 (26.14%), 37 (24.18%) and 22 (14.38%) showed moderate, high and extremely high risk of suicide in NGASR. As for PSQI, the median (range) was 9 (1-21) and there were 64 (41.83%), 39 (25.49%) and 20 (13.07%) reported not bad, average and poor sleep quality, respectively.

Relationship between psychological variables and clinical variables

Table 3 presented the relationships between psychological variables of the caregivers and clinical characteristics of relevant ALS patients. There was no noticeable relationship between gender, residence, smoking, drinking and occupation and any of PHQ-9, SAS, SDS, NGASR or PSQI of ALS caregivers ($p>0.05$). As presented in Figure 1, High educational level was significantly related to low PHQ-9 ($p=0.008$) or PSQI score ($p=0.047$). Pet raising and regular reading was significantly associated with low PHQ-9, SDS, NGASR and PSQI ($p<0.05$). Participation in ALS-related social activities was negatively related to NGASR of ALS caregivers

Table 1. Demographic characteristics of included ALS caregivers and relevant ALS patients

Items	ALS patients	Caregivers
Age (years old)	52.32 (13.42)	51.61 (12.67)
Gender (M/F)	93/60	79/74
Nationality (n, %)		
Han	152 (99.35%)	151 (98.70%)
Manchu	0 (0.00%)	1 (0.65%)
Hui	1 0.65%)	1 (0.65%)
BMI (kg/m^2)	22.23 (4.52)	
Onset (n, %)		
Bulbar	33 (21.57%)	
Upper limbs	87 (56.86%)	
Lower limbs	33 (21.57%)	
Disease duration (months)	18 (6-38)	
Baseline total MRC score	145 (91-159)	
Baseline ALSFRS-R score	40 (17-46)	
Follow-up ALSFRS-R score	26 (7-44)	

Note: The Shapiro-Wilk test was used to assess whether data exhibited a normal distribution. Normally distributed variables were expressed as means (standard deviation, SD) while abnormally distributed variables were expressed as medians (range).

Abbreviations: ALS amyotrophic lateral sclerosis; ALSFRS-R ALS functional rating scale-revised; BMI body mass index; F female; M male; MRC the Medical Research Council.

Table 2: Results of psychological scales in ALS caregivers

Scales	ALS caregivers (N=153)
PHQ-9 (n, %)	
0-4	30 (19.61%)
5-9	31 (20.26%)
10-14	37 (24.18%)
15-19	17 (11.11%)
20-27	38 (24.84%)
SAS (Standard score) (n, %)	
<50	89 (58.17%)
50-59	23 (15.03%)
60-69	34 (22.22%)
≥70	7 (4.58%)
SDS (Disease index) (n, %)	
<50%	56 (36.60%)
50%-59%	41 (26.80%)
60%-69%	33 (21.57%)
≥70%	23 (15.03%)
NGASR (n, %)	
≤5	54 (35.29%)
6-8	40 (26.14%)
9-11	37 (24.18%)
≥12	22 (14.38%)
PSQI (n, %)	
≤5	30 (19.61%)
6-10	64 (41.83%)
11-15	39 (25.49%)
≥16	20 (13.07%)

Abbreviations: ALS amyotrophic lateral sclerosis; NGASR the Nurses' Global Assessment of Suicide Risk scale; PHQ-9 the Patient Health Questionnaire-9; PSQI Pittsburgh sleep quality index; SAS Self-Rating Anxiety Scale; SDS Self-Rating Depression Scale.

($p<0.001$). Good financial status was related to high PHQ-9 score in caregivers ($p=0.013$) and financial support was negatively associated with PHQ-9 ($p=0.006$) and PSQI ($p=0.032$) of caregivers. Affordability for treatment was negatively related to PHQ-9 ($p=0.027$) and NGASR ($p=0.032$) of caregivers.

There was a negative correlation between disease duration of ALS patients and PHQ-9, SAS, SDS, NGASR, PSQI of their caregivers ($p<0.05$). Onset age of ALS was negatively related to PHQ-9 ($p<0.001$) and SDS ($p=0.003$) in ALS caregivers. Bulbar involvement in ALS patients was significantly related to high level of SDS in caregivers ($p=0.028$). Follow-up ALSFRS-R score was negatively related to while ALSFRS-R rate was positively related to the PHQ-9, SAS, SDS, NGASR and PSQI of caregivers ($p<0.05$). Less food intake of ALS patients was remarkably related to high levels of PHQ-9 ($p=0.003$) and SDS ($p=0.010$) of caregivers (Supplementary Figure 1).

Except for the lack of significant correlation between SAS and NGASR, analyses revealed predominant associations among all other involved psychological indicators regarding ALS caregivers ($p<0.05$).

DISCUSSION

In the study, we explored the prevalence of anxiety, depression, risk of suicide and poor sleep quality in ALS caregivers from Chinese mainland. Our results revealed that over 40% of ALS caregivers suffered from different degrees of depression and anxiety, which were comparable to the prevalence of Chinese ALS patients.[8,10] Data from Europe showed that around 1/4 of ALS caregivers might reported depression or anxiety[18,19], which was lower than our results. Besides, a considerable proportion of ALS caregivers reported suicidal tendency as evaluated by NGASR. Nearly 1/5 of included caregivers has planned suicide or have attempted suicide, which might be a serious social issue in China. Apart from the differences in sample size and psychological scales, the unsatisfactory healthcare system, insufficient social security system and high costs of the treatment might contribute to the high prevalence of depression, anxiety and suicide risk in Chinese ALS caregivers. Also, in China nursing care of ALS patients was generally performed by one caregiver, usually immediate families. Lack of support from other relatives or society made the caregivers tightly bound to the ALS patients. The heavy burden of care and negative emotions from ALS patients could significantly impact the caregivers' quality of life and result in high prevalence of anxiety, depression and suicide.

Our results revealed the close associations between the disease condition and functional status of ALS patients and their caregivers' psychological disorders. The earlier the patient's onset age and the shorter the course of the disease, the more suffering the caregivers might be. Also, our results indicated the negative impacts of ALS functional status and progression rate on the mental health of their caregivers, which were consistent with prior studies.[7,20-22] This emphasized

Table 3. Relationships between involved variables among caregivers of ALS patients

	PHQ-9		SAS		SDS		NGASR		PSQI	
Gender (M/F)	0.714		0.489		0.222		0.810		0.573	
Onset age of ALS patients	-0.313	**<0.001**	0.482		-0.242	**0.003**	0.168		-0.241	0.003
BMI (kg/m^2) of ALS patients	0.753		0.883		0.765		0.588		0.458	
Food intake of ALS patients	**0.003**		0.569		**0.010**		0.243		0.164	
Disease duration of ALS patients	-0.738	**<0.001**	-0.161	**0.047**	-0.715	**<0.001**	-0.469	**<0.001**	-0.533	**<0.001**
Bulbar involvement (Y/N)	0.141		0.803		**0.028**		0.582		0.876	
Follow-up ALSFRS score	-0.509	**<0.001**	-0.446	**<0.001**	-0.481	**<0.001**	-0.250	**0.002**	-0.439	**<0.001**
ALSFRS-R rate	0.366	**<0.001**	0.647	**<0.001**	0.356	**<0.001**	0.294	**<0.001**	0.325	**<0.001**
Financial status	**0.013**		0.747		0.293		0.838		0.076	
Financial support	-0.221	**0.006**	0.462		0.094		0.227		-0.173	**0.032**
Affordability for treatment	**0.027**		0.701		0.087		**0.032**		0.069	
Educational level	**0.008**		0.483		0.076		0.155		**0.047**	
Residence	0.452		0.640		0.063		0.479		0.072	
Smoking	0.082		0.503		0.067		0.300		0.441	
Drinking	0.112		0.748		0.215		0.421		0.815	
Pet raising	**<0.001**		0.069		**<0.001**		**<0.001**		**<0.001**	
Academic occupation	0.422		0.327		0.220		0.441		0.068	
Regular reading	**<0.001**		**0.003**		**<0.001**		**<0.001**		**<0.001**	
Participation in social activities	0.085		0.135		0.086		**<0.001**		0.058	
PHQ-9			0.234	**0.004**	0.860	**<0.001**	0.591	**<0.001**	0.595	**<0.001**
SAS					0.209	**0.009**	0.197		0.217	**0.007**
SDS							0.517	**<0.001**	0.522	**<0.001**
NGASR									0.508	**<0.001**

Note: Due to the abnormal distribution, Mann-Whitney U test or Spearman coefficient was used for the analysis. Significant data ($p<0.05$) were bold and relevant coefficients were presented.

Abbreviations: ALS amyotrophic lateral sclerosis; ALSFRS-R ALS functional rating scale-revised; BMI body mass index; MRC the Medical Research Council; N no; NGASR the Nurses' Global Assessment of Suicide Risk scale; PHQ-9 the Patient Health Questionnaire-9; PSQI Pittsburgh sleep quality index; SAS Self-Rating Anxiety Scale; SDS Self-Rating Depression Scale; Y yes.

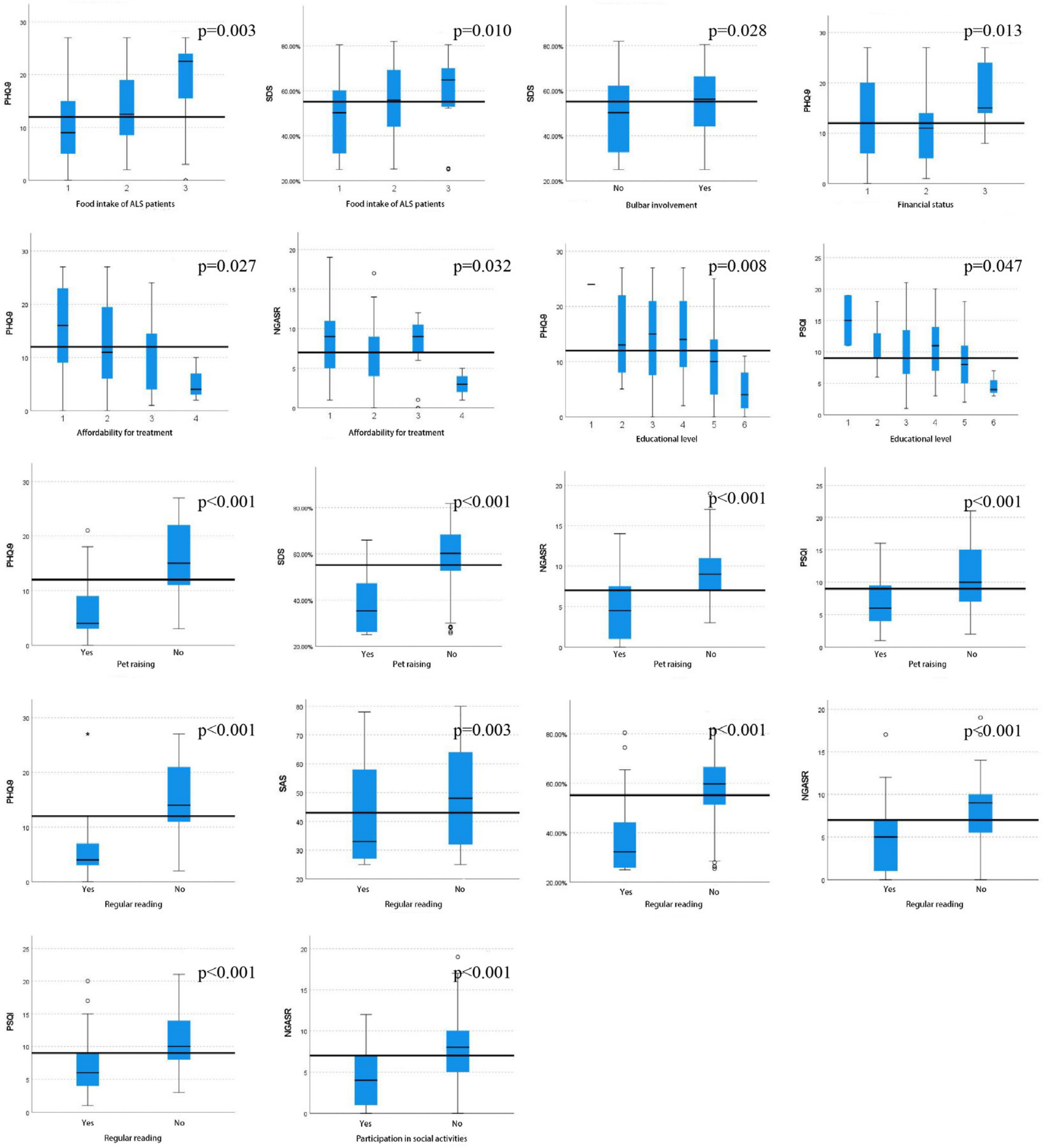

Figure 1. Significant results of nonparametric test.

Note: Food intake: normal (option 1), decrease of less than (option 2), no less than (option 3) half of the food intake compared to that before onset; Financial status: <5000 yuan/month (option 1), 5000-20000 yuan/month (option 2), 20000 yuan/month (option 3); Affordability for treatment: giving up treatment due to inability to afford the cost of treatment (option 1), costs of treatment significantly influence family lives (option 2), affordability of treatment with decrease of quality of life (option 3), no significantly financial burden caused by the treatment (option 4).

the importance of providing psychological support to the caregivers of ALS patients in the early stages of diagnosis, especially for those family members of early-onset ALS with rapid progression. With the prolongation of the disease course and the increase of knowledge of ALS, the caregivers might gradually accept the illness and accustomed to the care of patients. Aust Elisa and her co-workers reported serious emotional issues among ALS population in the advanced stages and their caregivers.[23] Continued increase of care burden and fear of death of the patients might be the causes, which also deserved attention. Less food intake and bulbar involvement might further increase the difficulty of care for the ALS patients, which give rise to the depression of caregivers.

As there was no effective treatment that could reverse ALS condition, we tried to find some alterable factors that could alleviate the psychological distress of ALS caregivers. Besides the lack of financial support and inability to afford ALS treatment, educational level and regular reading were closely associated with the mood of caregivers. Those with advance degree and regular reading were more easily accessible to knowledge regarding ALS and its care. They understandings of the meaning of life might be also different. Pet raising and participation in social activities might increase sense of belonging and provide emotional support, significantly lower the risk of suicide in ALS caregivers, which should be recommended to these participants. All in all, a more comprehensive social and medical security system in China should be established to provide more support for ALS caregivers. Also, medications and psychotherapy should be recommended to ALS caregivers if necessary.

Sleep disturbance was another problem for ALS caregivers, but relevant investigations were scarce. Our results suggested that over 80% of included caregivers suffered from poor sleep quality. Worries about the costs for ALS treatment was significantly associated with sleep disorders in ALS caregivers. Anxiety and depression also interacted with sleep disorders among ALS caregivers. To the best of our knowledge, there was no study utilizing polysomnography (PSG) to explore the disturbance of sleep of ALS caregivers and relevant pharmacological studies were scarce. More attention was deserved to help improve the sleep quality of ALS caregivers.

There are several limitations of this study. Firstly, the cross-sectional design did not allow us to explore the casual relationships between included variables. The incidence and changes of depression and anxiety among ALS caregivers after onset of ALS also needed further investigations. Secondly, the low response rate might result in selection biases. Not all approached caregivers agreed to participate, typically because of perceived lack of time or because they preferred not to think about MND and its effects. Thirdly, we only used questionnaires for ALS caregivers and all evaluations of ALS patients including ALSFRS-R score relied on their caregivers. Psychological status of ALS patients and its correlation with their caregivers' negative emotions was not included in the analysis. Last but not least, in order to shorten the filling time of the questionnaire, several variables including the quantitative assessment of care burden were excluded.[24] Ventilator support and artificial nutrition of ALS patients might significantly correlated with the psychological distress of their caregivers, which deserved future studies.

In conclusion, depression, anxiety, poor sleep quality and risk of suicide were commonly reported by ALS caregivers in a study based in Beijing, China. Early onset, bulbar involvement, poor functional status, rapid progression and lack of financial support may be associated with the psychological distress of ALS caregivers. Regular reading, pet raising and participation of social activities could alleviate the anxiety and depression, decrease risk of suicide and improve sleep quality of ALS caregivers.

DISCLOSURE

Ethics: The study was approved by the Ethics Committee of the Peking Union Medical College Hospital (PUMCH) (JS1210). All enrolled patients in our database provided written, informed consent to be included in the study.

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Conflict of interest: None

REFERENCES

1. Kiernan MC, Vucic S, Cheah BC, *et al*. Amyotrophic lateral sclerosis. *Lancet* 2011; 377(9769): 942-55. doi: 10.1016/S0140-6736(10)61156-7.
2. Masrori P, Van Damme P. Amyotrophic lateral sclerosis: a clinical review. *Eur J Neurol* 2020; 27(10): 1918-29. doi: 10.1111/ene.14393.
3. EFNS Task Force on Diagnosis and Management of Amyotrophic Lateral Sclerosis, Andersen PM, Abrahams S, Borasio GD, *et al*., 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.
4. Carvalho TL, Sanguinett de Almeida LM, Araujo Lorega CM, *et al*. Depression and anxiety in individuals with amyotrophic lateral sclerosis: a systematic review. *Trends Psychiatry Psychother* 2016; 38(1): 1-5. doi: 10.1590/2237-6089-2015-0030.
5. Lucia D, McCombe PA, Henderson RD, Ngo ST. Disorders of sleep and wakefulness in amyotrophic lateral sclerosis (ALS): a systematic review. *Amyotroph Lateral Scler Frontotemporal Degener* 2021; 22(3-4): 161-9. doi: 10.1080/21678421.2020.1844755.
6. Tramonti F, Bonfiglio L, Bongioanni P, *et al*. Caregiver burden and family functioning in different neurological diseases. *Psychol Health Med* 2019; 24(1): 27-34. doi: 10.1080/13548506.2018.1510131.

7. Schischlevskij P, Cordts I, Gunther R, *et al*. Informal caregiving in amyotrophic lateral sclerosis (ALS): A high caregiver burden and drastic consequences on caregivers' lives. *Brain Sci* 2021; 11(6). doi: 10.3390/brainsci11060748.
8. Huang S, Zheng MY, Lin JN, *et al*. Natural history and remarkable psychiatric state of late-onset amyotrophic lateral sclerosis in China. *Acta Neurol Scand* 2022; 146(1): 24-33. doi: 10.1111/ane.13598.
9. Stutzki R, Schneider U, Reiter-Theil S, Weber M. Attitudes toward assisted suicide and life-prolonging measures in Swiss ALS patients and their caregivers. *Front Psychol* 2012; 3:443. doi: 10.3389/fpsyg.2012.00443.
10. Chen DZ, Guo XY, Zheng ZZ, *et al*. Depression and anxiety in amyotrophic lateral sclerosis: correlations between the distress of patients and caregivers. *Muscle Nerve* 2015; 51(3): 353-7. doi: 10.1002/mus.24325.
11. Costa J, Swash M, de Carvalho M. Awaji criteria for the diagnosis of amyotrophic lateral sclerosis:a systematic review. *Arch Neurol* 2012; 69(11): 1410-6. doi: 10.1001/archneurol.2012.254.
12. Cedarbaum JM, Stambler N, Malta E, *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. doi: 10.1016/s0022-510x(99)00210-5.
13. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001; 16(9): 606-13. doi: 10.1046/j.1525-1497.2001.016009606.x.
14. Dunstan DA, Scott N, Todd AK. Screening for anxiety and depression: reassessing the utility of the Zung scales. *BMC Psychiatry* 2017; 17(1): 329. doi: 10.1186/s12888-017-1489-6.
15. Dunstan DA, Scott N. Norms for Zung's Self-rating Anxiety Scale. *BMC Psychiatry* 2020; 20(1): 90. doi: 10.1186/s12888-019-2427-6.
16. Cutcliffe JR, Barker P. The Nurses' Global Assessment of Suicide Risk (NGASR): developing a tool for clinical practice. *J Psychiatr Ment Health Nurs* 2004. 11(4): 393-400. doi: 10.1111/j.1365-2850.2003.00721.x.
17. Hartmann JA, Carney CE, Lachowski A, Edinger JD. Exploring the construct of subjective sleep quality in patients with insomnia. *J Clin Psychiatry* 2015; 76(6): e768-73. doi: 10.4088/JCP.14m09066.
18. Vignola A, Guzzo A, Calvo A, *et al*. Anxiety undermines quality of life in ALS patients and caregivers. *Eur J Neurol* 2008; 15(11): 1231-6. doi: 10.1111/j.1468-1331.2008.02303.x.
19. Pagnini F. Psychological wellbeing and quality of life in amyotrophic lateral sclerosis: a review. *Int J Psychol* 2013; 48(3): 194-205. doi: 10.1080/00207594.2012.691977.
20. Chiò 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. doi: 10.1212/01.WNL.0000162034.06268.37.
21. Creemers H, de Moree S, Veldink JA, Nollet F, van den Berg LH, Beelen A. Factors related to caregiver strain in ALS: a longitudinal study. *J Neurol Neurosurg Psychiatry* 2016. 87(7): 775-81. doi: 10.1136/jnnp-2015-311651.
22. Pagnini F, Rossi G, Lunetta C, *et al*., Burden, depression, and anxiety in caregivers of people with amyotrophic lateral sclerosis. *Psychol Health Med* 2010; 15(6): 685-93. doi: 10.1080/13548506.2010.507773.
23. Aust E, Linse K, Grauprier ST, *et al*. Quality of life and mental health in the locked-in-state-differences between patients with amyotrophic lateral sclerosis and their next of kin. *J Neurol* 2022; 269(11): 5910-25. doi: 10.1007/s00415-022-11238-0.
24. Felgoise SH, Chakraborty BH, Bond E, *et al*. Psychological morbidity in ALS: the importance of psychological assessment beyond depression alone. *Amyotroph Lateral Scler* 2010; 11(4): 351-8. doi: 10.3109/17482961003667630.