

Fatigue and Depression in Iranian Amyotrophic Lateral Sclerosis Patients in Tehran in 2012Maryam Nazemi¹, Marjan Hassani Raad², Christineh Serob Arzoomanian³, Azizreza Ghasemzadeh⁴

¹ Master in Personality Psychology, Education and Psychology Faculty, Islamic Azad University, Karaj Branch, Karaj, Iran

² Master in General Psychology, Education and Psychology Faculty, Islamic Azad University, Tehran Science and Research Branch, Tehran, Iran

³ Master in Clinical psychology, Education and Psychology Faculty, Islamic Azad University, Roudehen Branch, Roudehen, Iran

⁴ Lecturer in Rehabilitation Science, University of Applied Sciences, Tehran Welfare Organization, Tehran, Iran

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Abstract

Introduction: Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease with a progressive and rapid course. Fatigue and depression are common among ALS patients. The aim of this study was to determine the relationship between depression and fatigue in Iranian ALS patients.

Methods: In this 2012 cross-sectional study, 40 ALS patients, including 22 females and 18 males, were selected through consecutive relapsing-remitting, and 40 age- and gender-matched health controls (HCs) were recruited from Loghman Hakim Hospital in Tehran, Iran. The Persian version of the Fatigue Severity Scale (FSS-Per) questionnaire and depression substance of Hospital Anxiety and Depression Scale (HADS) were used to assess fatigue and depression. Data were analyzed using the Kolmogorov-Sminov Test, Levene's test, Independent Samples t-test, and Pearson product-moment correlation coefficient.

Results: We identified a significant and positive relationship between fatigue and depression in patients with ALS ($p=0.000$). Furthermore, the scores of fatigue and depression in ALS patients were higher than in non-ALS patients.

Conclusion: The results indicated that there was a relationship between fatigue and depression in ALS patients and that early intervention services can improve these symptoms. Further studies are suggested to investigate the direction of such relationship.

Keywords: Amyotrophic Lateral Sclerosis, Fatigue, Depression, Iran

1. Introduction

Defining Amyotrophic Lateral Sclerosis (ALS) as the "most common chronic neurodegenerative disorder of the motor system in adults," Ng and Khan stated that this disorder is a rare disease with a range of 0.0015 to 0.0025% throughout the world, with more men afflicted than women (the ratio of men to women was estimated to be 1.5) (1). They classified the symptoms as fatigue and depression, which impact on physical conditions. A 2006 research study by Stromberg & Weiss described a disease that results in some problems in respiration and can lead to death (2). Linking ALS to symptoms, such as fatigue and depression, they postulated that these symptoms play a crucial role in decreasing the patients' perception of the quality of life. In 2011, Vucic et al. enumerated some symptoms of ALS as fatigue and neurodegeneration, which are very frequent (3). They concluded that fatigue and weakness in ALS patients are significantly related to lower motor neuron dysfunction. The symptoms are so deeply destructive on patients that have very low-quality lives, and some of them prefer suicide and even euthanasia (4). Comparing depression in ALS and non-ALS patients, they found that this symptom is slightly higher in ALS patients but lower than among patients with MS. As the disease advances, patients feel that they are constrained in their abilities and,

Corresponding author:

Azizreza Ghasemzadeh. University of Applied Sciences, Tehran Welfare Organization, Tehran, Iran.

Tel: +98. 9331332853, E-mail: a.ghasemzadeh@irimc.org

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consequently, they show depression, anxiety, and other failures in mental status (5). Also, studying the effectiveness of psychological intervention, they concluded that the intervention could considerably reduce the levels of anxiety and depression in ALS patients (from 9.83% to 6.23%, with some margin of error). A 2011 survey by Attasi et al. named depression as a frequent symptom of ALS that affects all aspects of patients' lives. They recorded 11 depression-related symptoms in ALS patients, the most important of which were insomnia, fatigue, pain, and anxiety (6). Pagnini discussed that this fatal disease is continuing disorder that has huge impacts on patients and their caregivers (7). Epton et al. related ALS to hopelessness and depression and even their preferences about quality of life differ from those in non-ALS patients (8). The results of research by Lou et al. (2003) showed that patients with ALS, compared to non-ALS patients, presented more symptoms of fatigue and depression. In a study of 25 ALS patients using a questionnaire, they found that these two variables were significantly related to the poor quality of life (9). The present study was aimed at determining the relationship between depression and fatigue in Iranian patients with Amyotrophic Lateral Sclerosis (ALS).

2. Material and Methods

2.1. Research design and sampling

In this cross-sectional study, 40 ALS patients were selected between May 2012 and April 2013. They were asked to complete the research instruments, including the Hospital Anxiety and Depression Scale (HADS) and the Persian version of the Fatigue Severity Scale (FSS-Per). Afterwards, the data were analyzed using the Kolmogorov-Sminov test, Levene's test, and Pearson's correlation. The ALS patients included 22 females and 18 males who were selected through consecutive relapsing-remitting, and 40 age- and gender-matched health controls (HCs) were recruited from Loghman Hakim Hospital in Tehran, Iran.

2.2. Eligibility criteria

Eligible participants were patients with a clinical diagnosis of ALS defined as suspected, possible, laboratory-supported probable, or definite ALS based on McDonald's criteria (10). The patients had no other mental or physical disease or any relapse during the last three months before the assessment, and all of them that were seen at the Loghman Hakim Hospital's ALS clinic between May 2012 and April 2013 were asked to participate. Having selected the ALS group, those adults who were matched with regard to gender and age were included in the control group. In addition, appropriate mental health status (MALSE > 22) was taken into account as a criterion for HCs to be included into the study (11). Also, having no symptom of physical or mental disease was another cornerstone for them. In addition, patients who were new to the ALS clinic and came only for one second-opinion visit were excluded. Participants were given questionnaires related to fatigue and depression.

2.3. Measurement tools

Fatigue score was assessed using the Persian version of Fatigue Severity Scale (FSS-Per). The results indicated that all items had an internal consistency coefficient greater than 0.8 and a total Cronbach's alpha of 0.96. In addition, it was found that the FSS-PER score was in correlation with UPDRS score ($r=0.55$, $p<0.001$) and the "Hoehn and Yahr" (HY) stage ($r=0.48$, $p<0.001$). With regard to FSS-Per, it was found that it could significantly discriminate the IPD patients with more severe disability (HY stage > 2) from patients with severe disease (HY stage = 2) (AUC=0.81 (95% CI: 0.72-0.90)). Since the FSS-Per was proved to have a high internal consistency and construct validity, it can measure the severity of fatigue in IPD patients (12). The FSS-Per focused solely on the physical symptoms of fatigue, and it is the most commonly-used instrument to measure the severity of fatigue among individuals with ALS. Depression was measured with the Persian-validated depression substance of Hospital Anxiety and Depression Scale (HADS). Cronbach's alpha coefficient was reported as 0.78 and 0.86 for the anxiety sub-scale and depression sub-scale, respectively, of the Persian version of HADS. Using group comparison analysis, the validity of the scale was reported as being acceptable (12). The HADS contains 14 items and consists of two subscales, i.e., anxiety and depression, the latter of which was used in the present study. The FSS-Per and HADS were used as a self-report tool, but structured interviews were conducted with patients who had difficulty reading.

2.4. Research ethics

The study was approved by the Loghman Hakim Hospital Institutional Review Board. Also, the principles of ethics in research were approved, and the patients were informed of all stages in the study.

2.5. Data analysis

We used SPSS version 20 (IBM-SPSS) to analyze the data. The Kolmogorov-Sminov test was used to determine that the data were normally distributed. In addition, Levene's test and Independent Samples t-test were used to compare the variances of fatigue and depression in patients and HCs. Pearson's product-moment correlation coefficient was used to determine the relationship between fatigue and depression at the significance level of 0.05.

3. Results

The study included 40 ALS patients (22 females and 18 males) whose ages were between 30 and 50 with a mean of 32. They were recruited from Loghman Hakim hospital in Tehran, Iran, in 2012. The results showed that in the sample (n=80), 40 patients were suffering from ALS, among whom 22 were female and 18 were male. In addition, the Kolmogorov-Smirnov test was used to determine that the sample data were normally distributed. It was revealed that the Z-value was not significant for any variable at the level of $\alpha=0.05$, so normality of data variance was confirmed, and, consequently, we were able to use the parametric test. Pearson's correlation coefficient was used to examine the relationship between fatigue and depression in patients with ALS. The results showed that there was a significant and positive relationship between fatigue and depression ($r=0.66$, $p=0.000$, $n=40$). It can be inferred, therefore, that the increase in fatigue for patients with ALS would increase their depression. The mean and standard deviation for fatigue in the control group were reported as 25.40 and 3.11, respectively, which were less than those in patient group (mean=47.32, SD=8.64). In addition, the mean and standard deviation for depression in the control group were 4.57 and 0.696, respectively, which were less than the values for the patients (mean=7.95, SD=0.942). Table 1 shows that the variances for fatigue were not identical ($F=30.278$); thus, it can be referred to the significance at the second level ($p=0.000$, $\alpha=0.05$). With regard to fatigue, it was proved that there existed a significant difference between the two groups; in addition, comparing the means in the two groups, it was indicated that patients with ALS suffered more fatigue than the control group ($t=15.083$, $df=3.7$). Moreover, the variance for depression was reported to be the same in both groups ($F=2.443$). Furthermore, there was a significant difference in depression between two groups, which indicated that the patients suffered depression more than the control group ($t=18.240$, $df=4.16$).

Table 1. Results of Levene's test and independent t-test for two groups

| Groups | | Levene's test | | t-value | Degree of freedom | p-value |
|------------|-------------------|---------------|-------|---------|-------------------|---------|
| | | F | Sig. | | | |
| Fatigue | Equal variances | 30.278 | 0.000 | -15.083 | 78 | 0.000 |
| | Unequal variances | | | -15.083 | 48.982 | 0.000 |
| Depression | Equal variances | 2.443 | 0.122 | -18.240 | 78 | 0.000 |
| | Unequal variances | | | -18.240 | 71.820 | 0.000 |

4. Discussion

Aiming to examine the relationship between depression and fatigue in ALS in a selected group of samples, the findings of the present research showed that fatigue and depression was significantly related. Also, the correlation between fatigue and depression was confirmed in HCs. It is worth noting that the fatigue conditions in ALS and depression are distinguishable in the manner that the fatigue in ALS lasts for a short period of hours, whereas the one in depression can be prolonged for days. In addition, the ALS-related fatigue was deteriorated by heat, but the depression-related fatigue included sadness, anxiety, and hopelessness, which were not observed in ALS patients. The results are consistent with the 2014 studies by Jenkins et al. who indicated that the complaint of fatigue should prompt consideration of the cause, for example, early respiratory failure or malnutrition, which directs management. They concluded that similar to fatigue, poor sleep should prompt consideration of cause. Fragmented, unrefreshing sleep is an early sign of respiratory failure and responds to non-invasive ventilation (NIV). Poor sleep can also be due to depression, pain, or difficulty turning in bed because of truncal weakness (13). In addition, the research findings are comparable with those reported by McElhiney et al. (14), who examined the frequency and persistence of fatigue and depression and the relationship to the status of the ALS disease. Implementing the treatment on 223 patients by completion of the ratings, the results showed that 99 patients (44%) suffered from clinically significant fatigue, among whom 34 patients showed symptoms of depression. In addition, it was revealed that 16 patients had major or minor depression, whereas 108 patients showed no symptoms of depression or fatigue. Moreover, it was revealed that, although depression was not in association with the severity of ALS, fatigue had a relationship with that. Three months later, 33 patients who showed symptoms of fatigue in the first time still represented the same situation, while 10 patients showed depression. It's worth mentioning that the fatigue at the beginning was reported for 25 out of 113 patients, while the depression rate at the beginning was 7 out of 113

people. Nevertheless, the rates of depression and fatigue for 65 patients were reported stable in the third time. At the end, it was revealed that fatigue, compared to depression, had a greater frequency in patients with ALS and a greater association with the severity of ALS. Symptoms of fatigue and depression were reported to be independent mostly and influential on patients' treatment (14). Our findings are consistent with those of Matza et al., who examined the Fatigue Associated with Depression Questionnaire (FAsD) to assess fatigue and its impact among patients with depression. The results, collected over a six-week period, proved that the subscales of fatigue had influenced depression in different manners. In addition, the researchers found that there was a correlation between FAsD scores and Brief Fatigue Inventory change ($r = 0.73$; $p < 0.001$). It was revealed that some changes in FAsD could be imposed and the way respondents defined the changes might be effective in interpretation of changes in treatment. Therefore, it can be concluded that FAsD can be used as an effective instrument for measuring the symptoms of fatigue among patients with depression (15).

5. Conclusions

Fatigue plays a crucial role in ALS as a symptom of the disease process, but ALS increases by fatigue through depression. Furthermore, depression can be considered as the result of fatigue. Nevertheless, the exact direction of the cause and effect between fatigue and depression is beyond the research design. It can be concluded that fatigue and depression are significantly related, but further studies are suggested to investigate the direction of their relationship.

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Conflict of Interest:

There is no conflict of interest to be declared.

Authors' contributions:

All authors contributed to this project and article equally. All authors read and approved the final manuscript.

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