ΣΥΣΧΕΤΙΣΗ ΤΗΣ ΚΑΤΑΘΛΙΨΗΣ ΤΩΝ ΦΡΟΝΤΙΣΤΩΝ ΑΣΘΕΝΩΝ ΜΕ ΠΟΛΛΑΠΛΗ ΣΚΛΗΡΥΝΣΗ ΜΕ ΤΑ ΣΥΜΠΤΩΜΑΤΑ ΚΑΤΑΘΛΙΨΗΣ ΤΩΝ ΑΣΘΕΝΩΝ

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Περίληψη

Εισαγωγή: Η αξιολόγηση της κατάθλιψης σε ασθενείς με Πολλαπλή Σκλήρυνση (ΠΣ) και των αντίστοιχων φροντιστών τους και η διερεύνηση της επίδρασης των καταθλιπτικών συμπτωμάτων των φροντιστών στα καταθλιπτικά συμπτώματα των ασθενών και αντίστροφα.

Μέθοδος: Συμπεριλάβαμε δεδομένα από 94 ασθενείς με ΠΣ και τους φροντιστές τους. Αξιολογήσαμε την κατάθλιψη των ασθενών με ΠΣ και των φροντιστών τους, χρησιμοποιώντας την HAM-D (Κλίμακα Hamilton για την Κατάθλιψη). Η εκτίμηση του βαθμού αναπηρίας των ασθενών πραγματοποιήθηκε με την κλίμακα EDSS (Kurtzke Expanded Disability Status Scale).

Αποτελέσματα: Η κατάθλιψη στους φροντιστές ασθενών με ΠΣ συσχετίζεται αρνητικά με το μορφωτικό επίπεδο και θετικά με το γυναικείο φύλο. Στην πολυπαραγοντική ανάλυση παλινδρόμησης η κατάθλιψη των ασθενών συσχετίζεται αντίστροφα με το μορφωτικό τους επίπεδο (συντελεστής = -1.88; 95%CI -3.16, -0.61; p = 0.004) και θετικά με το βαθμό αναπηρίας τους (συντελεστής = 1.04; 95%CI: 0.49, 1.59; p < 0.001). Σε αντίθεση με τους φροντιστές, τα καταθλιπτικά συμπτώματα των ασθενών συσχετίστηκαν ανεξάρτητα με τα καταθλιπτικά συμπτώματα των φροντιστών (συντελεστής = 0,29, 95%CI: 0,11, 0,47, p = 0,002).

Συμπέρασμα: Τα συμπτώματα κατάθλιψης των φροντιστών, τα οποία φαίνεται να έχουν αρνητικό αντίκτυπο στην κατάθλιψη των ασθενών θα πρέπει να παρακολουθούνται προσεκτικά και να αντιμετωπίζονται, γιατί μαζί με την επιβάρυνση των φροντιστών οι ψυχολογικές δυσκολίες μπορούν να επηρεάσουν αρνητικά τον υποστηρικτικό τους ρόλο ενώ αυξάνουν τα καταθλιπτικά συμπτώματα των ασθενών με αρνητικό αντίκτυπο στην ποιότητα ζωής τους και προσαρμογή στην ΠΣ.

Λέξεις ευρετηρίου: πολλαπλή σκλήρυνση, αναπηρία, φροντιστές, κατάθλιψη

DEPRESSION IN CAREGIVERS OF PATIENTS WITH MULTIPLE SCLEROSIS IS ASSOCIATED WITH PATIENTS' DEPRESSIVE SYMPTOMS

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Abstract

Background and Purpose: To evaluate depression in a consecutive sample multiple sclerosis (MS) patients and their respective caregivers and to investigate the impact of caregivers' depressive symptoms to the patients' depressive symptoms and vice versa.

Methods: We included data from 94MS patients and their consecutive caregivers.We assessed the depression of MS patients and their caregivers using the HAM-D (Hamilton Scale for Depression). The disability status of the patients was assessed using the EDSS(Kurtzke Expanded Disability Status Scale).

Results: Depression in caregivers of MS patients is negatively correlated with education status and positively with female sex. In multivariable linear regression analysis on the association of baseline characteristics with patients' Hamilton scale scores the patients' depressive symptoms were also found to be inversely correlated with a higher education level(coefficient = -1.88; 95%CI -3.16, -0.61; p = 0.004) and positively associated with the patients' disability status, assessed with the EDSS score (coefficient = 1.04, 95%CI: 0.49, 1.59; p < 0.001). Opposed to caregivers, patients' depressive symptoms was independently correlated to the caregivers' depressive symptoms (coefficient = 0.29; 95%CI: 0.11, 0.47; p = 0.002).

Conclusion: Caregivers depressive symptoms, which seem to have a negative impact on patients' depression should be carefully monitored and treated, because together with burden and caregivers psychological difficulties can affect negatively their supportive role while increase patients depressive symptoms with negative impact in their quality of life and adjustment to MS.

Key words: multiple sclerosis, disability, caregivers, depression

Introduction

Patients with MS have an increased incidence of neuropsychiatric disorders, with depression being one of the most common among them (Henry et al., 2019), with a life-time prevalence estimated at around 50% (Papparigopoulos et al., 2010). MS patients seem to experience more frequently severe depression than patients affected by other severe neurological diseases (Wallin et al., 2006) with suicide rates two-fold higher compared to those reported in the general population (Bronnum-Hansen et al., 2005). Severe depression affects 15.7% of MS patients, compared with 7.4% in the general population and 9.1% in people suffering from other chronic disorders, suggesting a direct effect of MS on the depression (Henry et al., 2019). In a recent meta-analysis, the annual prevalence of a depressive episode is reported to be almost three times greater compared with the general population (17% versus 6%) while the mean prevalence was 30.5% (Boeschotten et al., 2017).

Depressive symptoms have an important negative impact upon quality of life (Feinstein et al., 2007), cognitive functions, adherence to treatment (Alba-Pale et al., 2017), compromised social functioning, and more somatic complains, increasing the need for health services (Henry et al., 2019) and increased suicide risk (Boeschotten et al., 2017). Although the causes of the high rates of depression in MS are not well understood, many factors are supposed to be implicated in its etiology: Brain lesions immunological changes, the unpredictable course of the disease, disability due to the disease, lack of social support and inadequate caregiving (Boeschotten et al., 2017). Depression is considered to be, after disability, the most important factor regarding the patients quality of life (Berrigan et al., 2016).

In a previous study (Petrikis et al., 2019), where these patients and their caregivers were also included, we found high rates of clinical depression in caregivers, with very severe depression (HAM-D score ≥ 23) reported in 12.2% (N = 16), severe depression in 3.8% (N = 5), and moderate depression in 9.2% (N = 12) of the caregivers. Depression was negatively correlated with both physical health status and mental health status, and positively correlated with fatigue and caregiver stress. The aim of the present study is to evaluate the impact of caregivers depression to the patients depressive symptoms and vice versa.

Materials and Methods

Setting, study design, and subjects

Ninety four patients with MS and their corresponding caregivers, wereprospectivelyenrolled in this study. Their baseline characteristics are presented in Table 1. The MS patients were recruited from the Department of Neurology, University Hospital of Ioannina, Greece from October 2016 to March 2017. The inclusion criteria for the patients were: (1) having a definite diagnosis of MS, (2) being stable at the time of the study (defined as no change in the Kurtzke Expanded Disability Status Scale [EDSS] in the 3 months prior to study enrolment), (3) needing a caregiver to help them in everyday life, and (4) able to understand the aim of the study and give informed consent. The exclusion criteria for the patients were: (1) acute phase or relapse of MS, (2) change in the EDSS score during the previous 3 months, (3) coexistence with another disabling disease not related to MS, (4) diagnosis of dementia according to Diagnostic & Statistical Manual of Mental Disorders -5 (DSM-V) criteria, (5) history of alcohol or substance abuse, or (6) refusing to give informed consent.

For the caregivers, defined as the persons who provided informal care on a regular basis, the inclusion

Table 1. Baseline characteristics of patients with multiple sclerosis and their corresponding caregivers

	Caregivers (n = 94)	Patients (n = 94)	p-value
Age (years, mean±SD)	52.2 ± 12.3	43.0 ± 12.0	<0.001
Females (%)	46.2%	62.2%	0.103
Education			
– ≤6 years	27.7%	16.0%	
– 7-9 years	12.7%	8.5%	
– 9-12 years	26.6%	39.4%	
– >12 years	33.0%	36.2%	
Profession			
– Household	10.6%	17.0%	
– Retired	31.9%	37.2%	
– State employee	12.8%	14.9%	
– Private employee	8.5%	8.5%	
– Freelance	17.0%	7.5%	
– Unemployed	5.3%	7.5%	
– Farmer	13.8%	3.2%	
– Student	0%	4.3%	
Years of care(mean ± SD)	9.5 ± 5.9	–	
Years since MS diagnosis (mean ± SD)	–	9.7±6.4	
EDSS score (mean ± SD)	–	3.9±2.0	
Hamilton score (mean ± SD)	7.8 ± 5.9	11.1 ± 6.3	<0.001

criteria were: (1) living with the patient and being responsible for his/her everyday care and well-being, and (2) not being paid for caregiving.

The complete study protocol was approved prior to study initiation by the Ethics Committee of the University Hospital of Ioannina. Written informed consent was obtained from all patients and caregivers prior to study enrollment.

Methods

Caregiver assessments

Caregiver depression was assessed using the Hamilton Scale for Depression (HAM-D). This scale consists of 21 items, with the score being based on the first 17: 8are scored on a 5-point scale ranging from 0 (not present) to 4 (severe), and 9 are scored from 0 to 2.For evaluating the HAM-D scores, we adopted the severity ranges for the HAM-D reported by Zimmermann et al. as follows: no depression (score of 0-7), mild depression (8-16), moderate depression [17-22], and severe depression (≥23). We used validated Greek versions of HAM-D (Stathopoulou et al., 2011).

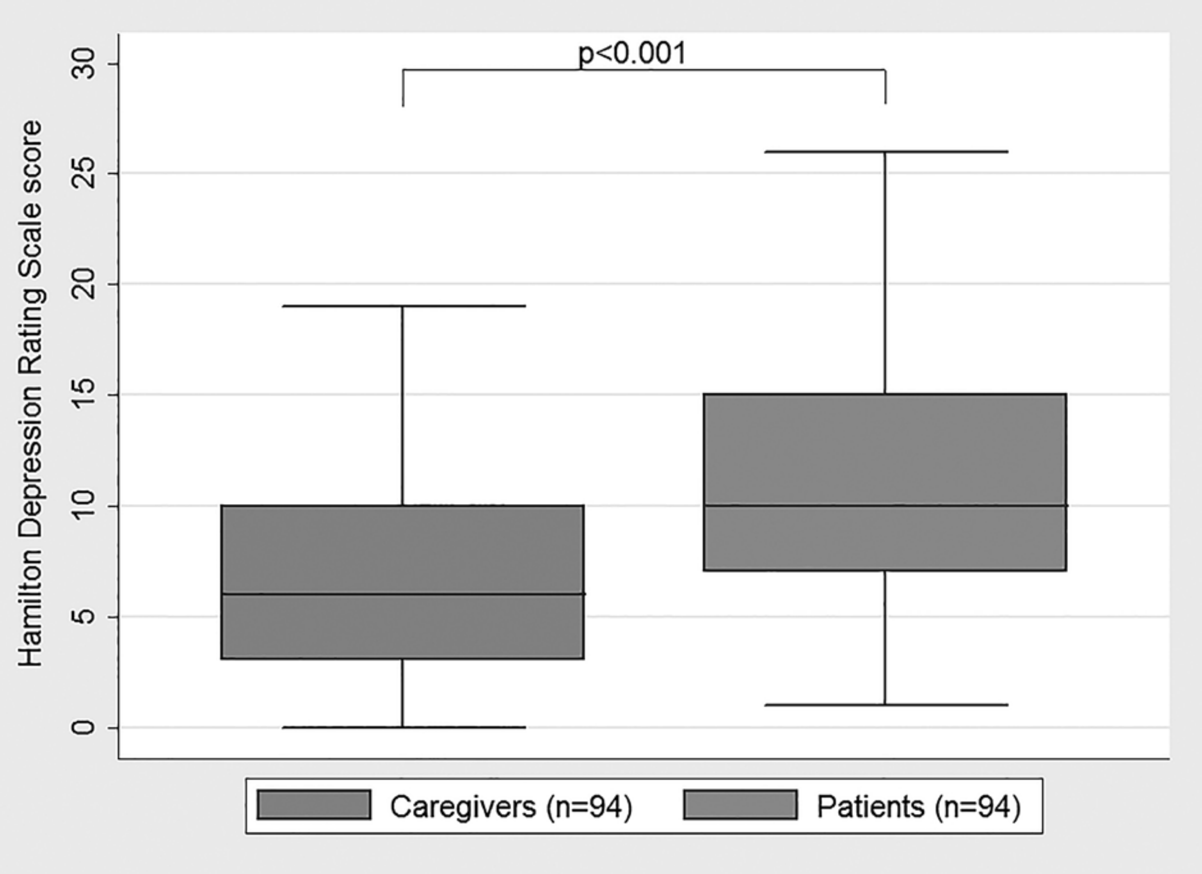
Patient assessments

– The EDSS was applied by an experienced neurologist to rate the disability status of each patient (Kurtzke et al., 1983).

Statistical analysis

We presented all dichotomous variables as percentages and continuous variables with their mean values and corresponding standard deviations. Baseline characteristics between patients and their caregivers were compared with the use of paired t-test (continuous variables) and McNemar test (dichotomous variables). We performed independent multivariable linear regression analyses for patients and their caregivers to investigate for potential correlations between available baseline characteristics and the depression status (assessed with the Hamilton depression scale) for each group. Per study protocol we also assessed with linear regression analysis the association of patients' Hamilton depression scale scores with the caregivers' Hamilton depression scale scores, and vice versa. All baseline characteristics that contributed to the outcome of interest in the initial univariable analyses at p values <0.1 were included in the multivariable model as candidate variables. The final variables that were independently associated in the multivariable regression analyses with the outcome of interest were selected by backward stepwise selection procedure using a p value <0.05. All statistical analyses

Figure 1. Hamilton Depression Scale scores of patients with multiple sclerosis and their corresponding caregivers



were performed with the use of the Stata Statistical Software Release 13 for Windows (College Station, TX, StataCorp LP).

Results

We had available data for 94 patients with MS and their corresponding caregivers. Compared to their caregivers MS patients were significantly younger (52.2 ± 12.3 vs. 43.0 ± 12.0; $p < 0.001$) and had higher Hamilton depression scale scores (11.1 ± 6.3 vs. 7.8 ± 5.9; $p < 0.001$; Figure 1). Other available baseline characteristics for both groups are presented in Table 1.

In multivariable linear regression analysis on the association of baseline characteristics with caregivers' depression status (Table 2), female sex (coefficient = 4.64; 95% CI: 2.53, 6.75; $p < 0.001$) and caregivers' level of education (coefficient = -1.02; 95% CI: -2.01, -0.03; $p = 0.043$) were found to be significantly associated with their depressive symptoms assessed with the Hamilton scale for Depression. Interestingly, no independent association between the caregivers' and patients' Hamilton scale scores was evident (coefficient = 0.14; 95% CI: -0.32, 0.32; $p = 0.108$).

In multivariable linear regression analysis on the association of baseline characteristics with patients' Hamilton scale scores (Table 3) the expressed patients' depressive symptoms were again found to be inversely correlated with a higher education level (coefficient = -1.88; 95% CI -3.16, -0.61; $p = 0.004$) and positively associated with the patients' disability status, assessed with the EDSS score (coefficient = 1.04, 95% CI: 0.49, 1.59; $p < 0.001$). Opposed to caregivers, patients' depressive symptoms was independently correlated to the caregivers' depressive symptoms (coefficient = 0.29; 95%CI: 0.11, 0.47; $p = 0.002$; Figure 2).

Discussion

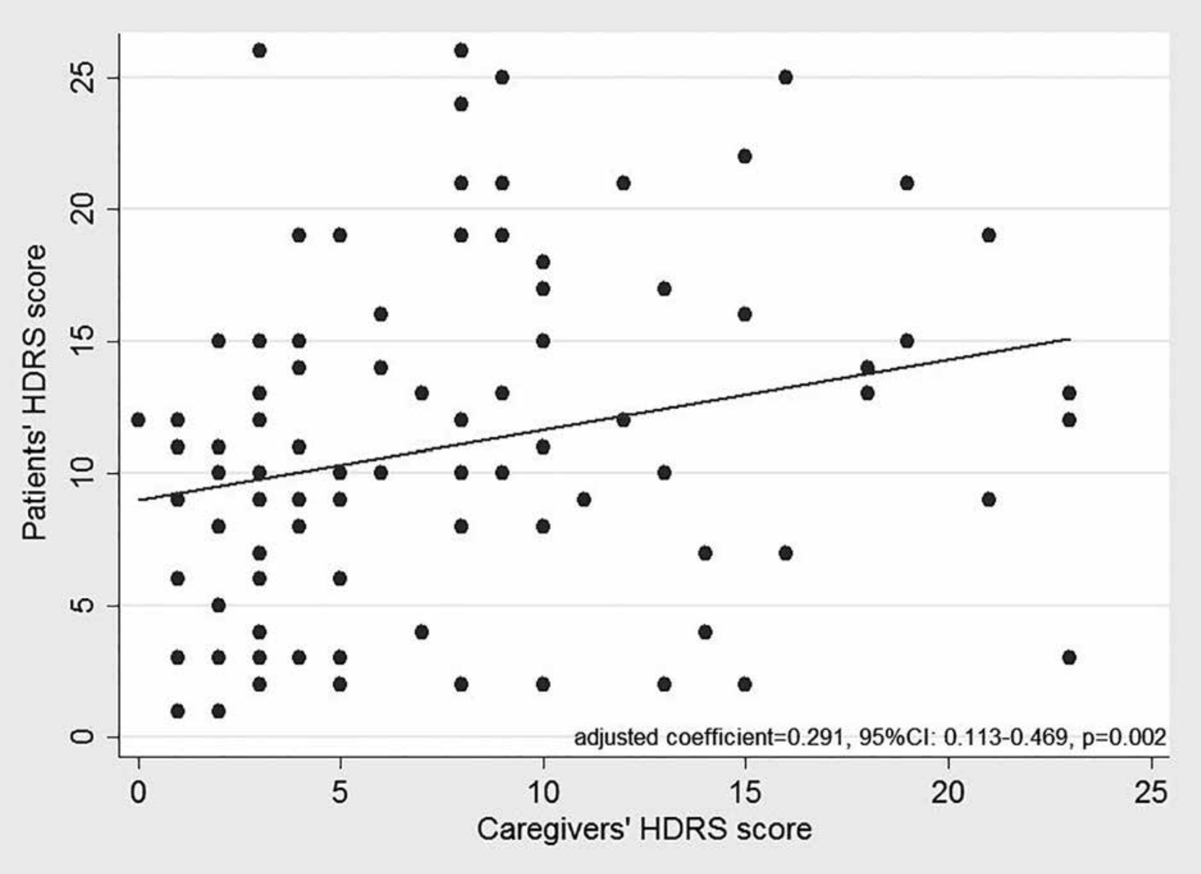
In this study we found caregivers depression to be positively associated with female sex and negatively associated with education level while patients' depression was positively associated with disability status and negatively associated with education level. Patients' depression –but not caregivers' depression– was independently correlated to the caregivers' depression.

The relationship between MS severity and depres-

Table 2. Univariable and multivariable linear regression analysis on the association of baseline characteristics with caregivers' depression status (assessed with the Hamilton Scale)

	UnivariableLinear RegressionAnalysis		**MultivariableLinearRegressionAnalysis**	
Variable	**coefficient (95%CI)**	**p**	**coefficient (95%CI)**	**p**
Age	0.092 (-0.005, 0.189)	0.062	0.533 (-0.047, 0.154)	0.296
Female sex	4.064 (1.852, 6.276)	<0.001	4.640 (2.533, 6.748)	<0.001
Education	-1.315 (-2.289, -0.342)	0.009	-1.019 (-2.007, -0.031)	0.043
Years of care	-0.073 (-0.280, 0.135)	0.488	-	-
Patients' Hamilton scale score	0.231 (0.044, 0.419)	0.016	0.143 (-0.319, 0.318)	0.108

Figure 2. Scatterplot on the association of Hamilton Depression Scale scores of patients with multiple sclerosis and the corresponding Hamilton Depression Scale scores from their caregivers



sion remains unclear, with some studies reporting a positive association (Chwastiak and Edhe, 2009) and others none (Möller et al., 1994; Pronvinciali et al., 1999). Recently, Kalron et al. (2018) reported a positive correlation between self-perception of walking and depression but not between quantitative gait parameters and depression. Ensari et al. (2017) found an association between depression and disability in MS patients while Lewis et al. (2017) found a direct relationship between actual disability and depression and perceived disability and suicide ideation.

Higher level of education is negatively associated in both patients' and caregivers' group with lower depression levels. Nakasawa et al. (2018) suggest a higher level of resilience as a possible explanation for lower depressive and anxiety symptoms in MS patients. Higher education could have a positive impact in psychological factors such as stress coping and self-esteem, notably associated with resilience.

Social support is of the utmost importance for patients in order to cope with stressful life events and has a positive impact on physical and mental health.

Table 3. Univariable and multivariable linear regression analysis on the association of baseline characteristics with patients' depression status (assessed with the Hamilton Scale)

	UnivariableLinear RegressionAnalysis		**MultivariableLinearRegressionAnalysis**	
Variable	**coefficent (95%CI)**	**p**	**coefficient (95%CI)**	**p**
Age	0.243 (0.147, 0.340)	<0.001	0.100 (-0.017, 0.217)	0.093
Female sex	-1.765 (-4.434, 0.902)	0.192	-	-
Education	-2.766 (-3.875, -1.658)	<0.001	-1.883 (-3.158, -0.608)	0.004
Years of MS	0.074 (-0.128, 0.276)	0.467	-	-
EDSS score	1.324 (0.722, 1.927)	<0.001	1.042 (0.494, 1.589)	<0.001
Caregivers' Hamilton scale score	0.265 (0.051, 0.480)	0.016	0.291 (0.113, 0.469)	0.002

It reduces morbidity and mortality and increases quality of life in the chronically ill. Significant others and especially caregivers are the most important social support providers (Henry et al., 2019).Poor perceived social support has been strongly correlated with depressive symptoms (Jensen et al., 2014; Henry et al., 2019). Caregivers with depressive symptoms possibly fail to respond properly to their supportive role. The depression of caregivers may have a direct effect and also an indirect, through their defective supportive role, in patients' depression.

Only two studies so far have investigated possible associations between MS patients and caregivers depression. Labiano-Fontcuberta et al. (2015) consider severity of MS patients depression to be a significant predictor of caregivers depression while Giordano et al. (2012) found in a sample of 251 persons that patients' depression was significantly associated with caregivers depression. Studies regarding other chronic disabling neuro-psychiatric disorders such stroke (Cameron et al., 2011), report that baseline depressive symptoms of caregivers were associated with more depressive symptoms in the patients' group (Klinedinst et al., 2009) while Cameron et al. (2011) found an association between patients' depression and family caregiver depression during the first two years of caregiving.

The cross-sectional study design and the limited sample size are two limitations of our study that preclude us from drawing general conclusions. Further studies in his direction will shed light to the complicated relationships between MS patients and their caregivers.

Conclusion

Caregivers depressive symptoms, which seem to have a negative impact on patients' depression should be carefully monitored and treated, because together with burden and caregivers psychological difficulties can affect negatively their supportive role while increase patients depressive symptoms with negative impact in their quality of life and adjustment to MS.

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