RESEARCH ARTICLE

Demographic and Clinical Characteristics of Persons with Multiple Sclerosis with Psychiatric Disorders

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Abstract

Objective: Psychiatric syndromes (PS) are among the most common comorbidities seen in multiple sclerosis (MS). It has been demonstrated that PS, such as depression, anxiety, and bipolar disorder, are more common in people with MS (pwMS) than in the general population. However, the reasons for this remain unknown. We aimed to identify the demographic and clinical characteristics of pwMS with PS and compare them with pwMS without PS.

Materials and Methods: In total, 2,732 (1,886 female; 846 male) pwMS attending the outpatient MS Clinic of Dokuz Eylul University Hospital were included in the study. We recorded the age, gender, disease duration, duration of PS diagnosis, age of onset, and MS course of the pwMS.

Results: PS had been diagnosed in 383 (14%) of pwMS, and in 352 of those it were diagnosed after their MS. There was no significant difference between the two groups in terms of disease duration and duration of diagnosis. There were significant differences regarding age, gender, age of onset, and MS classification between the two groups. The age and age of onset of PS in pwMS (45.89±11.50 and 30.42±9.81, respectively) were higher than in pwMS without a PS (44.09±12.57 and 29.29±9.74, respectively). The rate of female pwMS with a PS (76.4%) was higher than female pwMS without a PS (67.8%). Regarding the MS type, whereas 81% of those who had PS had relapsing-remitting MS (RRMS), 15.6% had secondary progressive MS (SPMS), and 3.4% had primary progressive MS (PPMS). Furthermore, 85.4% of those who had no PS were RRMS, 11% were SPMS, and 3.6% were PPMS.

Conclusion: In this study, the most related factors were age, gender, age of onset, and MS course for PS in MS. Studies involving other clinical features and cognitive functions are needed to better understand PS in MS.

Keywords: Multiple sclerosis, psychiatric syndrome, depression

Introduction

Multiple sclerosis (MS) is a chronic autoimmune disease characterized by central nervous system inflammation, demyelination, and axonal loss. Symptoms occur even in the early stages of the disease (1). MS is one of the most common causes of neurological disability in young and middle-aged adults and negatively affects their productivity and quality of life. Symptoms in MS differ according to the areas of involvement, and motor, sensory, cognitive, and neuropsychiatric symptoms are often observed (2,3).

Charcot first described the psychiatric syndrome (PS) seen in people with MS (pwMS) over a century ago (4). Recently, PS in MS has been discussed from epidemiological, clinical, and radiological perspectives (5).

Psychiatric symptoms are more frequent in pwMS than in people without it. Mood disorders, such as depression and anxiety are 20% more common. PS is often seen at the time of MS diagnosis and become more severe during the disease (6). Reports estimated that, on average, of pwMS with PS, 30% have depression, 22% anxiety, 13% bipolar mood disorder, 4% psychotic disorder, and 31% obsessive-compulsive disorder. These rates are high compared with the general population (7).

Considering the effects of psychiatric symptoms on cognitive performance, physical disability, and fatigue, early diagnosis

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of PS in pwMS improves their quality of life and increases compliance with treatment (5). In this study, we aimed to identify the demographic and clinical characteristics of pwMS with PS and compare them with pwMS without PS.

Materials and Methods

Study Design

This retrospective study was performed at the MS Clinic Dokuz Eylul University Hospital, Izmir, Turkey. This work has been approved by the Dokuz Eylul University Non-Invasive Research Ethics Committee (approval number: 2016/27-08, date: 20.10.2016). Informed consent was obtained from all participants.

Participants

The data of the participants who were diagnosed with MS were retrieved from the registry database, iMed (version 7.0.0; MSBase Foundation), and all participants were included in the study.

Outcome Measures

Demographic (gender, age, education level, marital status, employment status) and clinical data (date of onset, date of diagnosis, course of disease, age of onset of PS, and date of onset of PS) of pwMS were obtained from the medical records.

Statistical Analysis

The normal distribution of data was checked with the Kolmogorov-Smirnov test and histograms. Descriptive analyses are presented with mean and standard deviation for continuous variables and percentages for categorical variables. Logistic regression was performed to determine the risk factors for the participants with psychiatric disorders in pwMS. Statistical significance was set at $p<0.05$. Data were analyzed using the IBM SPSS Statistics software (Version25.0. Armonk, NY: IBM Corp.).

Results

In total, 383 (14%) of pwMS had a diagnosis of PS, and 352 of those were diagnosed with PS after their MS. There was no significant difference between the two groups in terms of disease duration and duration of diagnosis. There were significant differences regarding age, age of onset, gender, employment status, marital status, and MS classification between the two groups. The age and age of onset for pwMS with a PS were higher than that for those without a PS. The rate of female pwMS with a PS was higher than female pwMS without a PS. Regarding the MS type, while relapsing-remitting MS (RRMS) was more frequent in the pwMS with a PS, secondary progressive MS (SPMS) was more frequent in the pwMS without a PS (Table 1).

Logistic regression was performed to determine the effects of age, age of onset, gender, employment status, marital status,

and MS classification on the likelihood that pwMS would have PS. The logistic regression model was statistically significant: $x^2(6)=9.557$, $p<0.001$. The model explained 2.7% (Nagelkerke R^2) of the variance in having PS and correctly classified 85.3% of participants. The pwMS who were divorced and retired were 1.77 and 1.73 times, respectively, more likely to have a PS (Table 2).

Discussion

This study found a relationship between the diagnosis of PS in pwMS and age, age at onset, gender, employment status, marital status, and disease course. In all, 14% of our cohort received a PS diagnosis, most of which were made after the MS diagnosis.

Some studies have found no relationship between the duration of illness and PS diagnosis, consistent with the finding of this study. However, age and gender were not correlated, contrary to our results (8-10). We hypothesize that the high age and age at onset in the PS group may be due to it being more difficult to diagnose patients in this group.

The relationship between MS and PS diagnosis is complex. A pwMS may develop a PS because of the neuropathological process of MS or as a reaction to being diagnosed with MS (11). The etiology remains unclear. In this study, most pwMS who were diagnosed with PS received a psychiatric diagnosis later.

The rate of PS was higher in female pwMS than in males. Considering that PS such as depression are seen twice as often in society and the rate of women in MS is higher, this may be why the rate was higher in women (1,12). The rate of PS was higher in those with SPMS with higher disability. However, there are different results in the literature regarding the relationship between disability and PS (8,10).

Divorced pwMS was 1.77 times more likely to have a PS. Our study is consistent with reports that people with PS are more often single or divorced (13). Breslau et al. (14) showed that PS is related to divorce, and Landfeldt et al. (15) demonstrated that men with MS have an increased risk of divorce. In our cohort, the diagnosis of MS may have caused the divorce and triggered the PS. Another result of this study was that retired pwMS was 1.73 times more likely to have a PS. Considering the possibility of pwMS retiring early because of physical or psychiatric conditions, the increased risk may be due to this disease (16).

Study Limitations

The most important limitation of this study was that the PS were processed according to medical records. The study could have been made more robust by applying PS tests to the pwMS and evaluating their cognitive functions. However, this would have been difficult in such a large group of patients. Another

Table 1. Demographic characteristics of the participants (n=2732)

	PwMS with a psychiatric syndrome (n=383)	PwMS without a psychiatric syndrome (n=2349)	p-value
Age (years)	45.89±11.50	44.09±12.57	0.003
Age of onset (years)	30.42±9.81	29.29±9.74	0.038
Disease duration (years)	14.83±8.42	14.20±9.03	0.063
Time from symptom onset to diagnosis (days)	1174.60 (1644.30)	1153.28 (1686.59)	0.673
Gender			
Female	294 (76.8%)	1592 (67.8%)	<0.001
Male	89 (23.2%)	757 (32.2%)	
Employment status			
Unemployed	109 (36.7%)	600 (34.7%)	0.003
Employed	130 (43.8%)	848 (49.0%)	
Retired	41 (13.8%)	136 (7.9%)	
Student	17 (5.7%)	145 (8.4%)	
Level of education			
Primary school	75 (25.3%)	464 (27.2%)	0.675
High school	89 (30.0%)	474 (27.8%)	
College or university	133 (44.8%)	767 (45.0%)	
Marriage status			
Single	77 (26.1%)	479 (26.8%)	<0.001
Married	184 (62.4%)	1213 (68.0%)	
Divorced	34 (11.5%)	92 (5.2%)	
MS classification			
RRMS	311 (81.2%)	2005 (85.4%)	0.031
SPMS	60 (15.7%)	259 (11.0%)	
PPMS	12 (3.1%)	85 (3.6%)	

RRMS: Relapsing remitting multiple sclerosis, SPMS: Secondary progressive multiple sclerosis, PPMS: Primary progressive multiple sclerosis, PwMS: Person with multiple sclerosis

Table 2. Risk factors for having psychiatric syndromes in pwMS

Risk factors	OR	95% CI	p-value
Age (years)	0.998	0.981-1.015	0.803
Age of onset (years)	1.003	0.985-1.022	0.736
Gender (ref = female)			
Male	0.805	0.587-1.103	0.177
Employment status (ref = unemployed)			
Employed	1.087	0.791-1.494	0.608
Retired	1.729	1.083-2.761	**0.022**
Student	0.649	0.355-1.186	0.160
Marriage status (ref = single)			
Married	0.764	0.536-1.088	0.136
Divorced	1.768	1.046-2.987	**0.033**
Classification (ref = RRMS)			
SPMS	1.205	0.803-1.809	0.368
PPMS	0.924	0.448-1.908	0.831

Significant p-values are presented in bold. CI: Confidence interval, OR: Odds ratio, RRMS: Relapsing remitting multiple sclerosis, SPMS: Secondary progressive multiple sclerosis, PPMS: Primary progressive multiple sclerosis, PwMS: Person with multiple sclerosis, ref: reference variable

limitation is that the treatments of the patients were excluded from the study, since some MS treatments may trigger PS.

Conclusion

This study showed that several demographic and clinical factors are associated with a psychiatric diagnosis in pwMS. It also found that being retired and divorced increased the risk. The diagnosis and treatment of PS in pwMS is important to minimize the risk of adding another disease to their chronic condition and further impacting their quality of life.

Ethics

Ethics Committee Approval: This work has been approved by the Dokuz Eylul University Non-Invasive Research Ethics Committee (approval number: 2016/27-08, date: 20.10.2016).

Informed Consent: Informed consent was obtained from all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: E.K., Concept: O.S., H.K., E.K., Design: O.S., H.K., E.K., Data Collection or Processing: O.S., H.K., E.K., Analysis or Interpretation: O.S., H.K., E.K., Literature Search: O.S., H.K., E.K., Writing: O.S., H.K., E.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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