Prevalence of psychiatric disorders among patients with Multiple Sclerosis: a cross-sectional study.

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Abstract

Background: Multiple Sclerosis is one of the leading autoimmune disorders causing disability among young adults. Various types of mood, affect, and behaviour disorders along with cognitive impairment can be manifested in a course of MS, with affective and anxiety disorders being the most prevalent. Mental health challenges, in addition to the neurological burden of MS, significantly affect quality of life and the course of the underlying disease.

Objective: The aim of this work was to determine the prevalence of mental disorders in a sample of MS patients during outpatient treatment in Zabrze, Poland, with a focus on those with mood and anxiety disorders, and to compare the results obtained in these groups with clinical and sociodemographic data.

Method: The study was conducted between 2017 and 2018 on 103 MS patients of the Neurological Outpatient Clinic of the Medical University of Silesia Hospital No.1 in Zabrze, Poland. During the study, sociodemographic data were collected, as well as the type and course of the underlying disease, comorbidities, and medicines used. The MINI-international neuropsychiatric interview and a psychiatric examination were utilized to assess the occurrence of mental disorders.

Result: 68% of all patients received a psychiatric diagnosis at some point in their life with only 4% having been hospitalized before; 49.5% met the diagnostic criteria for various psychiatric disorders. Measured by the MINI International Neuropsychiatric Interview, 33% of patients reported a past episode of major depression while 8.7% met the criteria for a current episode. The same number of patients admitted ongoing treatment due to recurrent depressive disorder. In regards to anxiety disorders, the most common was generalized anxiety disorder (10.7%), followed by agoraphobia (8.7%), panic disorder (7.8%), and social phobia (4.9%). Most of the patients (94.2%) at the time of the psychiatric evaluation presented a low level of suicide risk, while 1.9% of the patients presented a medium risk, and 3.9% - a high risk.

Conclusion(s): The study confirmed a significantly higher prevalence of mental disorders among MS patients; thus, the psychiatric state of patients in this group should be investigated systematically, simultaneously with the assessment of their neurological state. Trial registration: N/A Key words: Multiple Sclerosis, psychiatric disorders, comorbidity, psychiatric care, clinical characteristics.

Background

Multiple Sclerosis is one of the leading autoimmune disorders, with around 2–3 million people living with this diagnosis across the globe (1). The geographical distribution of MS is not homogenous and varies widely depending on region, with a general rule of increased incidence along with increased distance from the equator, though there are exceptions (2). The reasons for this are widely debated (3). As the majority of affected individuals are in their early adult life, MS has a huge impact on quality of life and is one of the most common causes of a nontraumatic neurological disability in this age group in Europe and Northern America (4). MS is also a heterogenous disease in its course; thus, various degrees of worsening during the progressive phase can be observed, as well as various degrees of activity of

pathological processes in the relapsing phase (5) (6). The very moment of receiving the diagnosis is a stressful, life-changing event for the majority of patients and their families. To improve the quality of life of the patients, recognition of this emotional and cognitive burden is crucial in regards to all parties involved (7) (8).

Various types of mood, affect, and behaviour disorders along with cognitive impairment can be manifested in a course of MS, however some of them are understood as direct consequences of the ongoing brain damage resulting from multiple areas of axonal demyelination (9), while others are classified as varied psychological reactions to the progressing and disabling course of the disease (10) (11). The pattern of their development is still debated, however clinicians agree that these two categories usually overlap and are not, in any case, exclusive (12) (13). Cases of pure neuropsychiatric manifestations of MS are occasionally reported and show that the symptoms presented by patients are not specific, therefore, final diagnosis is often delayed because the diagnostic process is focused firstly on the primary psychiatric condition (14) (15) (16).

Much published research focuses on the prevalence of comorbid psychiatric disorders, in particular mood disorders, with the first studies conducted in the field in the 1920s (17). Major depressive disorder is especially common among MS patients. Studies show lifetime prevalence on a level varying between 24% and 50%, which is substantially higher than in the general population and in most other neurological disorders (13) (18) (19) (20) (21). In addition, higher rates of completed suicide are observed in this study group (22). Lifetime prevalence of anxiety disorders was reported on a level between 21–36% (23) (13) (24). Other less frequently reported mental disorders are bipolar affective disorder, psychosis, euphoria, pseudobulbar affect, and personality change (25) (13). Even though neurological and psychiatric manifestations are developed by MS patients with a higher prevalence than in the general population, they are usually overlooked in clinical settings (26) (27).

All of the mental disorders reported have a negative impact on disability developing progressively in relation to MS. Significantly lower quality of life, higher levels of fatigue, as well as lower levels of adherence to therapy are the main elements connected to psychiatric comorbidity in MS patients (28) (29).

The aim of this work was to determine the prevalence of mental disorders in a sample of MS patients during outpatient treatment in Zabrze, Poland, with a focus on those with mood and anxiety disorders, and to compare the results obtained in these groups with clinical and sociodemographic data.

Materials And Methods

This study involved 103 patients with a previously confirmed diagnosis of MS according to the McDonald criteria (30). These criteria are recommended by the Polish Multiple Sclerosis Society and were revised on a global level in 2017 (31). All patients were recruited while attending a follow-up treatment in an outpatient specialist clinic in the Neurological Department of the Medical University of Silesia Clinical Hospital No1 in Zabrze, Poland between January and December 2017. Inclusion criteria were: literacy,

signed, informed consent for participation in the survey, age between 18 and 70 years old, and a formal diagnosis of multiple sclerosis during a treatment process. Exclusion criteria were: illiteracy, withdrawal of consent or refusal to participate in the survey, age outside the set limit, a degree of disability > 8.0 on the Expanded Kurtzke Disability Status Scale (EDSS), and cognitive impairments which would prevent proper understanding of the course and nature of participation in the study including a history of brain injury and stroke.

The study protocol for this cross-sectional research was presented to the Bioethics Committee at the Medical University of Silesia and received a thorough approval (No. KNW/022/KB1/136/16). All patients selected to join the study were shown a comprehensive summary of the aims and goals of the study, tools used by the researchers, and information processing conditions. Written consent was given to the participants to sign and they were informed that it can be withdrawn at any time without consequences to their basic treatment process. Medical history with a focus on sociodemographic data and medications was gathered along with a clinical assessment performed by a neurology specialist to evaluate disability status through the Expanded Kurtzke Disability Status Scale (EDSS) (32). Then, in the next stage, qualified MS patients were referred to psychiatrists to conduct a full psychiatric evaluation. The main diagnostic tool was the MINI International Neuropsychiatric Interview (version 6.0) that allows clinicians to assess for the 15 most common psychiatric disorders included in the DSM-IV and ICD-10 (33) (34). A separate section of this diagnostic instrument allowed for the evaluation of suicide risk within the studied group. In addition, a clinical psychiatric examination was conducted to supplement the results obtained in the questionnaire.

Statistical analysis was performed using R environment version 3.3.2. Data obtained by measurement were expressed as arithmetical mean ± standard deviation and quartiles, and those obtained by counting were expressed as a percentage. Pearson's χ2 test with Yates's correction for continuity was performed for categorical univariate analysis. Student's t-test was used in comparing patient groups for the score of normal distribution and equal variances, whereas Welch's test was employed when the null hypothesis in Fisher's test for variances was rejected. The Mann-Whitney U test was performed for scores that did not exhibit normal distribution. P < .05 was regarded as significant.

Results

In total, 103 patients qualified for the study over the course of a year, with none of them withdrawing consent once given. The studied sample consisted of 70 (67.96%) female and 33 (32.03%) male patients. The age ranged from 18 to 66 years, with a mean of 43 (SD = 12.05). The duration of MS treatment ranged from below one year to 30 years, with a mean of 5.9 (SD = 5.64). The duration of MS symptoms ranged from below one year to 40 years, with a mean of 10.85 (SD = 8.75). The degree of disability ranged from 0.5 to 8.0, with a mean of 3.2 (SD = 1.61). The most common form of this disease, relapsing–remitting form, was found in 89 (86.40%) MS patients, while primary progressive form was found in 3 (2.91%), and secondary progressive in 11 (10.67%). The majority of patients, 97 (94.17%), had more than 20 areas of demyelination detected in an MRI scan. The number of neurological

hospitalizations within the group ranged from 1 to 50, with a mean of 4.74 (SD = 7.53). 56 (54.36%) patients were being treated additionally due to other somatic illness. 5 (4.85%) patients reported an elementary level of education (8 years), 21 (20.38%) patients finished vocational school (12 years), 37 (35.92%) graduated from secondary school (12 years), and 40 (38.83%) people had a higher education (up to 18 years). 55 (53.39%) patients reported being professionally active at the time of the study (Table 1).

Table 1
Basic clinical data of the MS respondents.

	number of respondents	average	standard deviation (SD)	median	min	max
Age	103	43.07	12.05	43	18	66
Duration of MS treatment	103	5.92	5.64	4	0	30
Duration of MS symptoms	103	10.85	8.75	8	0	40
Degree of disability (EDSS)	103	3.2	1.61	3	0,5	8
Number of neurological hospitalizations	103	4.74	7.53	2	1	50

Regarding the frequency of psychiatric disorders within the group as measured by the MINI International Neuropsychiatric Interview, the most common were diagnoses from the groups of mood and anxiety disorders. As regards the first group, mood disorders, 33% of patients reported a past episode of major depression while 8.7% met the criteria for a current episode. The same number of patients admitted ongoing treatment due to recurrent depressive disorder. A past manic/hypomanic episode was reported by 3.9% of patients, and bipolar disorder by 2.9%. None of the patients met the criteria for a current manic/hypomanic episode or reported past mood disorders with psychotic features. In regards to anxiety disorders, the most common was generalized anxiety disorder (10.7%), followed by agoraphobia (8.7%), panic disorder (7.8%), social phobia (4.9%), obsessive-compulsive disorder (2.9%), and posttraumatic stress disorder (1.9%). For other mental disorders, we had 3 patients reporting past psychotic disorders, current psychotic disorder, and harmful use of alcohol, while 2 other patients from the group were diagnosed and treated due to bulimia nervosa. Among those in the studied group, alcohol addiction, psychoactive substance addiction/harmful use, anorexia nervosa, antisocial personality, and intellectual disability were not detected (Table 2). In regards to suicide risk, most of the patients (94.2%) at the time of the psychiatric evaluation presented a low level of suicide risk, while 1.9% of patients presented a medium risk and 3.9% - a high risk. In comparison, in the clinical psychiatric examination, the most frequent psychiatric disorders diagnosed according to the International Statistical Classification of Diseases and Related Health Problems (ICD-10) were depressive episodes (F32) and organic mood disorders (F06.3) (24.3%), followed by anxiety disorders (F41) (11.7%), and adjustment disorders (F43.2)

(10.7%). In addition, mild cognitive disorder (F06.7) (7.8%), bipolar affective disorder (F31) (2.9%), and schizophrenia (F20.0) (1.9%) were present (Fig. 1).

Table 2
Psychiatric disorders in patients with multiple sclerosis, using the MINI International Neuropsychiatric Interview.

Psychiatric disorder	Number	%
Current episode of major depression	9	8.7
Past episode of major depression	34	33.0
Current manic/hypomanic episode	0	0.0
Past manic/hypomanic episode	4	3.9
Panic disorder	8	7.8
Agoraphobia	9	8.7
Social phobia	5	4.9
OCD	3	2.9
PTSD	2	1.9
Alcohol addiction	0	0.0
Harmful use of alcohol	1	1.0
Addiction to other psychoactive substances	0	0.0
Harmful use of other psychoactive substances	0	0.0
Current psychotic disorders	1	1.0
Past psychotic disorders	1	1.0
Current mood disorders with psychotic features	1	1.0
Past mood disorders with psychotic features	0	0.0
Anorexia nervosa	0	0.0
Bulimia	2	1.9
Generalized anxiety disorder	11	10.7
Antisocial personality	0	0.0
Recurrent depressive disorder	9	8.7
Bipolar disorder	3	2.9
Intellectual disability	0	0.0

In the study, the general demographics and clinical characteristics of patients experiencing current and past affective disorders and affective disorders with coexisting anxiety disorders (from the group of diagnoses F33 and F40-43) were examined and compared. The results showed no statistical significance in terms of gender. Also, the acquired data showed no significance in regards to age, duration of the disease, and scoring obtained on the EDSS scale (Graph 1, 2, 3).

Discussion

Most of the published studies assessing the prevalence of psychiatric disorders in multiple sclerosis patients were conducted in the countries of the northern hemisphere (Europe and the USA being the leading centres of research in the field) with a variety of limitations resulting also from the different tools used for analysis of psychiatric diagnosis (validated and non-validated questionnaires, structured interviews, medical records, administrative data) and diverse binding statistical classifications of psychiatric disorders (the International Statistical Classification of Diseases and Related Health Problems, the Diagnostic and Statistical Manual of Mental Disorders, the International Classification of Primary Care) (13). In addition, many of the published systematic reviews focus solely on the incidence and prevalence of depressive and/or anxiety disorders, determining either symptoms (scale studies) or disorders as Axis I diagnoses (35) (19). Few published studies used structured interviews to assess the prevalence of the most common psychiatric disorders in line with the Diagnostic and Statistical Manual of Mental Disorders. De Cerqueira et al. (22) evaluated 60 patients with MS in Brazil using version 5.0 of the Mini International Neuropsychiatric Interview (MINI) for the main diagnoses from the DSM-IV. In regards to affective disorders, the results showed that 36.6% of respondents had depression over the course of their life (18.3% past depressive episode, 18.3% current depression at the time of the study), while 13.3% had bipolar disorder (BD). In regards to anxiety disorders, the most common was generalized anxiety disorder (GAD) diagnosed in 16.7% of respondents, while the second most common was panic disorder (PD) detected in 3.3%. Other disorders from the anxiety axis were absent (22). Our study, by using a very similar study protocol and tools, also confirmed that the mood and anxiety disorders are the most prevalent among MS patients, however we noted a higher percentage of depressive episodes throughout life, a lower percentage of bipolar disorders, as well as a more diverse spectrum of anxiety disorders in comparison to Cerquiera et al. Attention should be paid to the 54% of patients with MS who were simultaneously treated for additional somatic diseases, which could affect the severity and increase the incidence of mental disorders (36).

Because the study concerned patients with changes in the structure of the CNS, the questionnaire method was supplemented by a psychiatric examination, which allowed for the diagnosis of clinical psychopathological symptoms characteristic of organic changes and mood disorders that did not meet the criteria for diagnosis in the MINI questionnaire. Almost the entire study group was diagnosed with demyelinating lesions in the CNS which were revealed through the MRI examination. This is a very important etiological factor that can initiate, exacerbate or sustain the existence of mental disorders (most often cognitive disorders) (37). Other causes of comorbidity of mental disorders include adaptation difficulties related to limitations, symptoms and social problems associated with MS, genetic

susceptibility, structural brain abnormalities, the association between depression and immunological and inflammatory changes, drug therapies causing psychiatric disorders, and personality traits that predispose an individual to the occurrence of mental disorders and diseases (38) (13). However, Gasim et al. presented in their work that there is no correlation between MS treatment and an increased risk of psychiatric symptoms caused by disease-modifying therapies (DMT) (39). The conducted psychiatric examinations of the discussed group revealed the occurrence of depressive disorders, detailing depressive episodes or organic mood disorders in 24% of MS patients, anxiety disorders in 11.9%, depressive disorders related to stress in 10.7%, and cognitive disorders in 7.8%. In other studies and reports, cognitive impairment affects 43−70% of the group. The small number of respondents who were found to have cognitive impairment in a psychiatric examination may be associated with the failure to use additional tools and tests to detect cognitive impairment, beyond interview and medical examination; this is one of the important limitations of this work. Reports analyzing the occurrence of mental disorders in MS only on the basis of a medical examination are few and the results obtained correspond to the results of the current work (40).

Galeazzi et al. evaluated 50 patients with relapsing-remitting MS in Italy using the SCID-I to diagnose lifetime and current Axis I psychiatric disorders. In regards to affective disorders, the results showed that 46% of respondents had depression over the course of their life, 6% had bipolar disorders, and 10% had dysthymic disorders. In regards to anxiety disorders, 36% of respondents had any of the anxiety disorders, with simple phobia being the most common (12%) (41). Marrie et al. evaluated 253 patients with MS using the SCID-I to diagnose Axis I Disorders and classified 10.3% as having major depression and 14.6% as having generalized anxiety disorder (42). Antmann et al. evaluated 166 patients with MS to compare self-reported outcome measures in identifying major depression, modifying the SCID telephone interview as a standard, with 29% of respondents meeting the criteria for MDD in terms of the SCID criteria (43). Feinstein et al. examined 100 patients with clinically defined MS attending yearly neurological examinations with the Structured Clinical Interview for DSM-IV and the results obtained showed that 17% of subjects met the criteria for diagnosis of major depression (44). Korostil and Feinstein evaluated 140 patients using the SCID-I to diagnose anxiety disorders, which were determined to be at a level of 35.7% throughout the lifetime of respondents, with generalized anxiety disorder at 18.6%, panic disorder at 10%, and obsessive compulsive disorder at 8.6% (45). Our study is so far the first in Poland to assess the prevalence of psychiatric disorders among MS patients using a structured interview with diagnostic criteria consistent with the DSM-IV. The results obtained seem to follow the general trend observed in other studies, however no statistical significance was observed in comparing the general demographics and clinical characteristics of patients experiencing current and past affective disorders, and affective disorders with coexisting anxiety disorders, in terms of gender, age, duration of the disease, and scoring obtained on the EDSS scale. Sorisoy et al. showed that MS patients with neurological disability and loss of ambulation are more prone to depression, and identified a correlation with EDSS determining degree of disability and depression scores (46). On the other hand, Janssens et al. found that MS patients and their partners continued to have high levels of anxiety and distress in the first years after diagnosis, however

there was no correlation with disability (47). Gottberg et al. also published a study proving that patients with depressive symptoms did not perform worse in different aspects of functioning (48).

Suicide risk studied within our group was low among the majority of respondents, while 1.9% of the patients presented a medium risk and 3.9% - a high risk. These results are relatively lower than what has been published by Sorisoy et al. In this sample, 8.3% had a past history of attempted suicide and 8.3% presented a current suicide risk; all patients presenting a current suicide risk had major depression at the time of the interview. (46) Feinstein et al. found a past suicide attempt in 6.4% of the patients interviewed (49). In the Danish group studied by Brønnum-Hansen et al., suicide risk among persons with multiple sclerosis was more than twice that of the general population, with increased risk particularly high during the first year after diagnosis (50). The risk of a suicide attempt in patients with MS is most often the result of the symptoms of depression, which result from the difficulty in coping with the symptoms of the disease, problems in everyday functioning, and lack of support (8) (51). Psychiatric comorbidities may also contribute to maladaptive coping strategies, and poor health behaviors which could alter the course of MS (52).

Lifetime prevalence of psychiatric disorders in the general adult population (aged 18–65) in the European Union countries incl. Norway, Iceland and Switzerland according to the WHO is 25%. 27% had experienced at least one of a series of mental disorders in the past year (this included problems arising from substance use, psychoses, depression, anxiety, and eating disorders) with 1 out of 15 people suffering from major depression, and if all anxiety and different forms of depression are included, 4 out of 15 people (53). Epidemiological studies conducted in Poland in 2015 by Kiejna et al. show that major depressive disorder was found in 3.0% of the population; it was significantly more frequent in women (4.0%) than in men (1.9%). Prevalence in men was not age-related, while in women major depressive disorder occurred significantly more frequently after the age of 50 (5.5%) than in women aged 18–29 (2.7%) and 30–39 (3.3%). Lifetime generalised anxiety disorder was found in 1.1% of the studied population, significantly more often in women (1.5%) than in men (0.6%) (54). This shows that the prevalence of mood and anxiety disorders is significantly higher in Poland than in the general population.

The most important limitations of this work are the small group of respondents with different forms of MS as well as a lack of accurate assessment of the severity of depressive disorders and cognitive impairment. The study did not exclude patients in the condition of exacerbation of the underlying MS disease, which could have influenced the number of patients meeting the criteria for the diagnosis of a specific mental disorder. We also recognize the limitations of this study resulting from data obtained through the MINI while the ICD10 is the most-used classification method in the country and medical records of the patients, along with the clinical psychiatric examination performed, are provided on the basis of the latter. In addition, we are aware of the multilateral model of mental health condition of the MS patients and the need of the more holistic assessment. (55)

Conclusion

The study confirmed a significantly higher prevalence of mental disorders among MS patients; thus, the psychiatric state of patients in this group should be investigated systematically, simultaneously with the assessment of their neurological state. Literature analysis and the current work confirm the need for a detailed diagnosis of co-occurring problems of MS patients in order to determine the optimal, personalized therapy plan.

Abbreviations

DSM = Diagnostic and Statistical Manual of Mental Disorders; DMT = disease-modifying therapy; EDSS = Expanded Disability Status Scale; ICD = International Classification of Diseases; MS = multiple sclerosis.

Declarations

Ethics approval and consent to participate

The study protocol for this cross-sectional research was presented to the Bioethics Committee at the Medical University of Silesia and received a thorough approval (No. KNW/022/KB1/136/16). All patients selected to join the study were shown a comprehensive summary of the aims and goals of the study, tools used by the researchers, and information processing conditions. Written consent was given to the participants to sign and they were informed that it can be withdrawn at any time without consequences to their basic treatment process.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

MB: research leader, design of the study, literature searches and analyses, statistical analyses, interpretation of data, manuscript writing

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Authors' information (-)

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Figures

Psychiatric disorders

Legend:
- None
- Adjustment disorders F43.2
- Anxiety disorders F41
- Depressive episode F32, organic mood disorders F06
- Schizophrenia F20
- Mild cognitive disorder F06.7
- Bipolar affective disorder F31

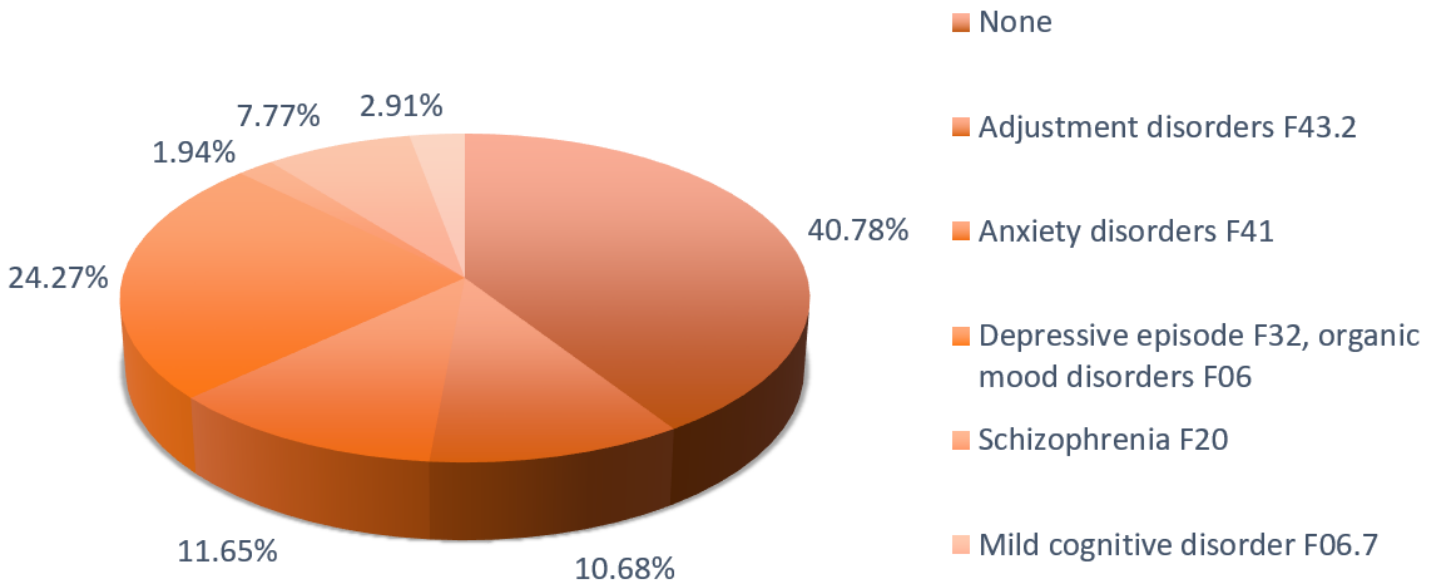Values: 40.78%, 10.68%, 11.65%, 24.27%, 1.94%, 7.77%, 2.91%

Figure 1

Psychiatric disorders in patients with multiple sclerosis, using the clinical psychiatric examination

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Graph1BlachutSM.docx
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- Graph2BlachutSM.docx