Characterizing Pain and Mental Health in Patients with Multiple Sclerosis Chronic Disease

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Abstract
MS is a chronic immune-mediated disease of the central nervous system that often leads to long-term physical disability. Thus, the long-lasting chronic disease affects the mental health and quality of people who have MS. Many researches have been conducted on the topic of MS with various psychological factors and symptoms. Yet, despite the increase in the associations of symptoms and quality of life of MS patients, it has received considerable attention in characterizing pain. However, there was still little understanding of the association of pain with mental health quality of life. Therefore, this study was presented to explore the characterization of pain and mental health in patients with MS chronic disease. A sample has been gathered from 199 patients diagnosed with MS from the Neurology clinic in Bangalore. By using various statistical tools, the results of a study have been analyzed. The result showed that the pain experienced significantly more severe symptoms of depression and anxiety, which were significantly worse for the mental health quality of life of patients. Further, it showed that past pain reported the highest percentage than the current pain of MS patients.
Keywords: Multiple sclerosis (MS), Pain, Mental health, Patients, Long-lasting disease, Depression, Anxiety.

1. Introduction

All over the world, Multiple Sclerosis has been considered as one of the most extensive disabling neurological conditions of young adults. It is a chronic disease of the nervous system, which generates several symptoms and may lead to critical psychological implications and severe disability [1]. The MS can be characterized by inflammation, demyelination, gliosis, and axonal loss. The course of MS chronic disease is extremely unforeseeable and varies between patients [2, 3]. MS also has comorbidities that can cause long-term health complications. The symptoms presented in MS diseases include vision problems, sensory disturbances, fatigue, cognitive deficits, motor deficits, spasticity, bladder, bowel dysfunction, pain, and depression, all of which can occur in different combinations [4]. Among all the symptoms of MS, pain and depression were the most frequent and prevalent comorbid condition reported symptoms of MS. Thus, the presence of pain and depression is a significant determinant of cognitive performance and may also impact the ability of person and functioning of patients, limit the ability to work, self-manage their condition and quality of life; thus, it leads to affect the mental health of patients [5, 6, and 7]. A diagrammatic representation of the symptoms of MS was shown in Figure 1,

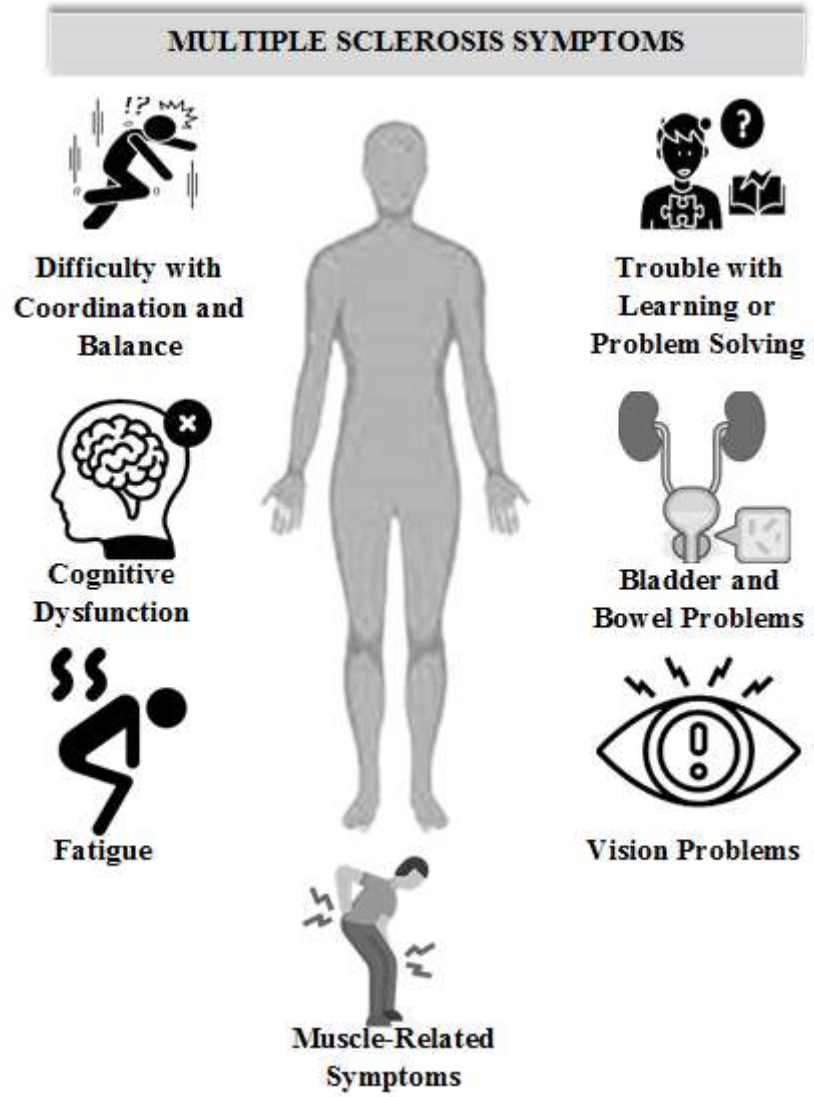

Figure 1: Common symptoms of MS

However, after the first years of MS diagnosis, the adaption to MS chronic disease becomes more emotionally challenging. Compared to general populations, MS patients experience psychological distress and are at higher risk of anxiety and depression due to symptoms of neurological [8, 9, and 10]. Some existing studies have reported the depression and fatigue associated with health-related quality of people. However, the association between pain, depression, and mental health-related quality of people with MS is necessary. However, to the best of our knowledge, exploring the characterization of pain and depression of patients with MS is still sparse. Thus, the present research study was intended to analyze the characterization of pain and mental health in patients with MS chronic disease. The main objective of this study is to explore the association between the pain in MS and depression, anxiety and quality of life of patients.

The structure of the paper is enlisted as follows: section 2 represents the existing literature review, the materials and methods are presented in Section 3, section 4 represents the result and discussion of the analysis, and Section 5 concludes the paper with future research scope.

2. LITERATURE REVIEW

Diana Ferraro *et al.* [11] intended to analyze the chronic pain characteristics of patients with MS. A sample has been taken from 374 enrolled MS patients. A collected sample and clinical data have been analyzed by using the Kruskal-Wallis test and Mann-Whitney test. The study concluded that neuropathic pain was a highly frequent type of chronic pain and it was associated with the sensory functional system involvement of 23.7%. A certain limitation has occurred in this study; first, to identify the spasticity-related pain, related tools lacked in this study, second, patients with higher pain intensity have been excluded due to the exclusion of moderately and severely depressed patients.

Claudio Solaro*et al.* [12] explored the prevalence of pain in MS patients and distinguished the various types of pain with MS. Data were gathered from six Italian MS centers; and then, by using a multi-center and cross-sectional study, a collected sample has been analyzed. Based on the classification of the DN4 score and clinical evaluation, the result indicated that 286 syndromes of nociceptive pain and 184 syndromes of neuropathic pain have been identified. However, the participation of MS outpatients was distributed along with Italian centers, which might be generalizable to other geographical countries.

TurhanKahraman*et al.* [13] investigated the distribution of pain, type, and frequency-related factors in persons with MS. Further, it explored neuropathic pain in persons with MS (pwMS). In this study, a sample of 223 pwMS patients was collected and analyzed through a pain DETECT questionnaire and a Nordic musculoskeletal questionnaire. Finally, it concluded that the majority of the patients has musculoskeletal pain (55.6%), and neuropathic pain was obtained by 21.1% of patients, while 23.3% of participants do not have pain. This study was based on a single center; thus, these factors decreased the generalizability of the findings.

HenrikHeitmanna*et al.* [14] identified the determinants and longitudinal prevalence of pain in multiple sclerosis. A sample has been collected from 410 MS patients in the German National MS cohort study. Then, to identify the biopsychosocial associations of pain, a linear regression analysis was applied. The study demonstrated that the prevalence of any type of pain has baselines at 40% and 36% after four years, whereas the Neuropsychiatric were strongly linked to depression, fatigue, and disability. However, in this study, the multivariate regression overlaps a clinical symptom and the biopsychosocial assessment factors were incomplete in this study.

Emine Rabia Koc*et al.* [15] examined the mental health and quality of life in patients with MS and health controls (HC) during the COVID-19 pandemic. Data has been taken from 86 MS patients and 65 HC patients. Then, to compare the normally distributed data and non-normally distributed data, an independent samples t-test and Mann-Whitney U tests have been employed. The result indicated that the energy and vitality ($p=0.018$), restriction rates ($p=0.006$), and pain ($p=0.005$) were significantly lower than those with EDSS$\leq$3. However, the collected samples were limited in this study.

AfaghGarjani MD *et al.* [16] intended to analyze the prevalence of long COVID-19 among people with MS patients. The participants of data were considered from the national cohort of people with MS and COVID-19 from the United Kingdom (UK) MS register (UKMSR). The result has been analyzed through multivariable Cox regression analysis. Thus, the result indicated that compared to pre-COVID-19, the prior COVID-19 participants with anxiety and

depression were less likely to report recovery from COVID-19. In this study, retrospective data collection has been used, which might affect the bias of the report.

Claudia H. Marck*et al.* [17] identified the modifiable lifestyle factors of depression, fatigue, mental health, anxiety, and quality of life associated pain in people with MS. An online survey of questionnaire data had been collected from 2,362 people with MS. By using multivariable regression analysis, the result of a study has been analyzed. The result indicated that there was a clear association between modifiable lifestyle factors and substantial pain in MS. However, this study was based on a cross-sectional design; thus, it couldn't assume temporal or causal relationships.

3. MATERIALS AND METHODS

The presented study analyzed the characterization of pain and mental health of MS long-lasting chronic disease patients. Further, it explored to assess the prevalence and type of pain in patients with MS and depression, anxiety and quality of life. A study sample has been gathered from 199 patients diagnosed with MS from the Neurology clinic in Bangalore from January 2023 to March 2023. The MS group was selected from patients who had been previously diagnosed, had regular outpatient follow-ups, and voluntarily accepted to participate in the study. The course of MS, namely relapsing-remitting (RR), primary progressive (PP), and secondary progressive (SP) of patients were considered in this study.

Then, the MS specialists evaluated the patients' EDSS scores. Here, the patient's demographic profile was analyzed. Both the demographic and clinical questionnaire of data has been completed on patients, including demographic profiles. A questionnaire has exhibited good test-retest reliability and validity in people with MS. Under the standard test circumstance, all the tests were assessed in the same fixed order.

Data Analysis

Using the Hospital Anxiety and Depression Scale (HADS) assessed depressive symptoms and anxiety, which is a self-assessment questionnaire scale. Then, by using Expanded Disability Status Scale (EDSS), the patient's pain and its association with mental health have been analyzed. The questions were based on depression and anxiety, and for each question, a score has been added to obtain results. Here, a total score of 0 to 7 represents no abnormalities, 8 to 10 represents a borderline score, and ≥11 indicates anxiety and/or depressive symptom. Based on an analysis of medical documentation and interview, the course of the disease was determined.

Statistical Analysis

The data were expressed as mean ± standard deviation (M±SD) and median with range or percentages. Moreover, the Chi-square test, Shapiro-Wilk test, t-test, or Mann-Whitney U test has been employed for the analysis of the results. Then, to investigate the associations between pain in patients, depression, anxiety, and mental health quality of life has been investigated through multivariable logic regression models, each adjusted for confounders of age, gender, disease duration, and type of MS.

3.1. Pain characteristics and patients characteristics of demographic and clinical features of MS patients

The demographic profile of respondents has been collected and analyzed. Here, the collected sample of patients had different forms of MS and some had clinically isolated syndrome.

Thus, the demographic and clinical characteristics of enrolled patients were shown in Table 1.

Table 1: Demographic and clinical features of MS patients along with pain characteristics

Patients	**N=199**
Age (years) (M ± SD)	49.2±13.1
Gender	
M (n, %)	81 (40.70)
F (n, %)	118 (59.29)
MS form	
RR (n, %)	97 (48.74)
PP (n, %)	39 (19.59)
SP (n, %)	53 (26.63)
CIS (n, %)	10 (5.02)
Disease duration (years) (M± SD)	14.4±8.8
Immunomodulatory/suppressive treatment	
Yes (n, %)	110 (55.27)
No (n, %)	89 (44.72)
EDSS (mean ± SD)	2.5±2.4
EDSS (median, interquartile range)	2.5 (1-4)

Table 1 represents the demographic characteristics and clinical characteristics of MS patients along with the pain characteristics. Here, age, gender, MS form, disease duration, immunomodulatory/suppressive treatment, and EDSS have been calculated and analyzed with mean, standard deviation, and percentage of an analysis. The obtained M ± SD value of the age category is 49.2±13.1. The gender can be categorized into male (M) and female (F); here, the majority of the respondents were female and the obtained percentage is 59.29%, whereas the percentage of male respondents is 40.70%. Then, by analyzing the MS form, the majority of the respondents are RR (48.74%), followed by SP (26.63%), PP (19.59%), and CIS (5.02%). Furthermore, the majority of the patients selected "yes" to the immunomodulatory/suppressive treatment (55.27%). However, the achieved mean and standard deviation of duration disease (years) and EDSS are 14.4±8.8 and 2.5±2.4, respectively, whereas the median of EDSS is 2.5.

4. RESULT AND DISCUSSION

In this section, the collected samples were thoroughly examined and the results were presented and discussed in detail. This section focused on two key aspects of the intention of pain among MS patients, associations of depression, anxiety, mental health, and quality of life with pain, and associations of health outcomes of long-lasting MS disease.

4.1. Intensity of pain among MS patients

The pain of various causes is a common phenomenon in patients with Multiple Sclerosis (MS). In 23% of patients with MS, pain was found as part of the presenting symptoms at disease onset. The occurrence of pain among MS patients has been analyzed, which was shown in Table 2 [6].

Table 2: Analysis of the occurrence of pain

Occurrence of pain	**Current pain report N (%)[a]**	**Current pain intensity [0÷10] M±SD**	**Past pain report N (%)[a]**	**Past pain intensity [0÷10] M±SD**	**P[b]**
Headache	81 (40.70%)	5.1±1.9	84 (42.21%)	6.2±2.4	R=0.69 P<0.0001
Back pain	70 (35.17%)	5.3±2.3	93 (46.73%)	6.1±2.2	R=0.85 P<0.0001
Pain in one or more extremities	75 (37.68%)	5.5±2.1	85 (42.71%)	5.2±2.1	R=0.89 P<0.0001
Muscle pain	57 (28.64%)	5.4±2.2	69 (34.67%)	5.8±2.5	R=0.83 P<0.0001
Facial pain	33 (16.58%)	5.3±2.2	40 (20.10%)	5.7±2.7	R=0.67 P=0.293
Lhermitte's sign	43 (21.60%)	4.7±2.9	55 (27.63%)	5.5±2.8	R=0.99 P<0.013

Here, the occurrence of the pain of a headache, back pain, pain in one or more extremities, muscle pain, facial pain, and Lhermitte's sign has been considered. The current pain and past pain of MS patients have been reported and its intensity has been analyzed in this section. 40.70% of patients highly reported headache in current pain and its intensity value is 5.1±1.9 followed by Pain in one or more extremities (37.68%), Back pain (35.17%)), Muscle pain (28.64%), Lhermitte's sign (21.60%), and Facial pain (16.58%). Then, by analyzing pain reported in the past, all the pain in MS patients achieved the highest percentage than the pain reported in the present. There is a significant relationship between the association of current pain and past pain; also, the occurrence of pain had significantly higher in Lhermitte's sign, and the obtained value is R=0.99 (P<0.013).

4.2. Associations of depression, anxiety, mental health, and quality of life with pain

After the diagnosis of MS's long-lasting disease, patients experience pain and have symptoms of depression and increased anxiety, and mental health problems. Here, the association of pains with depression, anxiety, mental health, and quality of life with pain has been examined from the collected samples, which were represented in Table 3 [6].

Table 3: Analysis of associations with pain

Associations	**Examined patients (N=199)**	**Current pain**		**P[b]**
		Yes (N=163)	**No (N=36)**	
	M±SD	**M±SD**	**M±SD**	
HADS-D [0÷21]	6.1±4.7	6.3±4.4	3.9±3.8	P<0.013
HADS-A [0÷21]	7.9±4.8	8.2±4.7	5.5±4.8	P<0.013
EQ-5D [0÷15]	8.1±2.3	8.3±2.0	6.6±1.6	P<0.0001
EQ-VAS [0–100%]	69.7±20.3	67.9±16.8	77.9±17.9	P<0.013

The associated symptoms of depression, anxiety, mental health, and quality of life of patients were explored with a questionnaire of depression symptoms HADS-D, anxiety symptoms HADS-A, Quality of life EQ-5D, and Mental Health EQ-VAS. The majority of the patients were reported to have the current pain. It revealed that patients who had reported current pain consummated additional severe symptoms of depression (P<0.013) and anxiety (P<0.013), which had significantly worse mental health (P<0.013) and quality of life (P<0.0001). Thus, the analysis of the mental health of the examined patients achieved the highest mean ± SD value, which is 69.7±20.3. A graphical representation of mean and SD values of associations of symptoms with current pain was shown in Figure 2,

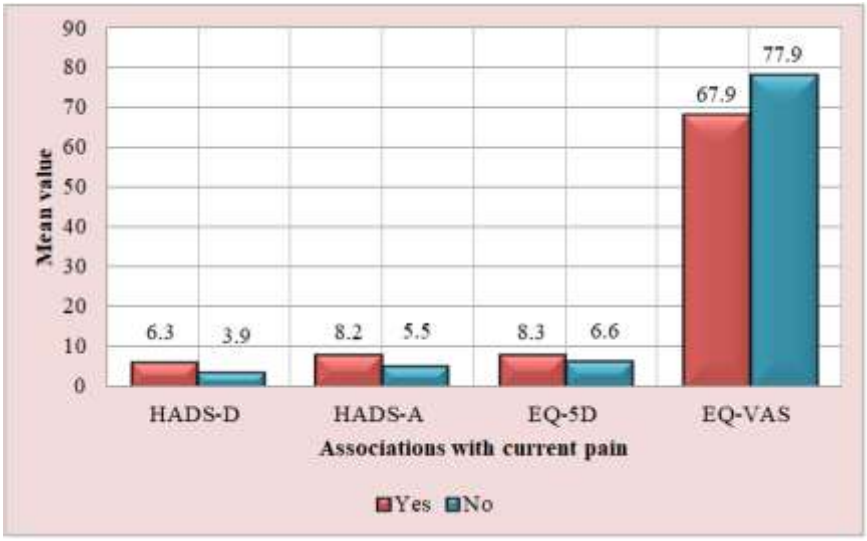

Figure 2: Associations of symptoms with current pain

4.3. Associations of health outcomes with substantial pain of long-lasting MS disease

Pain has strong links to the prevalence of anxiety and depression due to the long-lasting MS chronic disease of patients. Thus, maintaining a healthy lifestyle is difficult for those with MS as they have a higher risk of having poor health and developing other conditions.

Table 4: Analysis of associations of patient health outcomes

Patient health outcome	**Category**	**Number (%)**	**Adjusted odds ratio (95% confidence interval)**
Depression	Positive	69	Reference
	Negative	130	4.07 (3.23, 5.24)
Anxiety	Yes	53	Reference
	No	146	6.79 (4.95, 9.44)
Mental health QOL	N=199	68.1(67.3-69.9)	-16.7(-17.9 to -13.6)

Adjusted for age, gender, duration of MS, and quality of life

Table 4 represents the results of the association of health outcomes of quality of life with substantial pain of long-lasting MS disease [17]. The adjusted odds ratio score was calculated for the association of depression, anxiety, and mental health quality of life (QOL). In depression, 69 respondents were reported to be positive for the associations of patients' health outcomes and its adjusted odds ratio value is 4.07 (3.23, 5.24) and anxiety is 6.79

(4.95, 9.44). However, these two associations significantly affect the mental health QOL and the obtained value is -16.7(-17.9 to -13.6).

5. CONCLUSION

This study was intended to analyze the characterization of pain and mental health quality of life with MS and explored the associations between pain with depression, anxiety, and mental health. This study concluded that the current pain reported more severe symptoms of depression ($P<0.013$) and anxiety ($P<0.013$), which had significantly worse mental health ($P<0.013$) and quality of life ($P<0.0001$). Moreover, it also stated that the occurrence of headaches reported the highest percentage in current and its intensity of mean value is 5.1. Thus, when compared to pain reported in the current, the highest percentages are achieved by the pain reported in the past with significant associations. Moreover, the association of mental health QOL (-16.7(-17.9 to -13.6)) is highly associated with the pain of MS. However, this study was limited to the size of the sample and the symptoms to affect the mental health QOL of MS patients. In the future, this can consider more samples and explores the various associated factors and their significance levels in quality of life. This study leads hopes to potential application in pharmaceuticals and suggests serving as a therapeutic target for MS treatment.

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