

RESEARCH ARTICLE

A Survey of Severity and Distribution of Musculoskeletal Pain in Multiple Sclerosis Patients; a Cross-Sectional Study

Masoud ShayestehAzar, MD; Mohammad H Kariminasab, MD; Majid Sajjadi Saravi, MD; Mahmoud Abedini, MD; Mehran Fazli, MD; Seyyed Abbas Hashemi, MD; Pedram Abdizadeh, MD

Research performed at Imam Khomeini Hospital, Mazandaran University of Medical Sciences, Sari, Iran

Received: 11 November 2014

Accepted: 1 February 2015

Abstract

Background: Pain, a common phenomenon in multiple sclerosis (MS) patients, is associated with many symptoms and problems.

Aim: To investigate severity and distribution of musculoskeletal pain in MS patients.

Methods: In this cross-sectional study, 115 members of the Mazandaran MS Association with confirmed MS were randomly selected to participate in the study. The patients were asked to fill out Numerical Rating Score and Nodric questionnaires, respectively. The data was analyzed by SPSS ver. 16 software.

Results: The mean age of the participants was 30.43 ± 5.86 years and 88 cases (76.5%) were female. The mean disease duration was 26.34 ± 24.32 months and 87.8% of the cases were experiencing pain at the time of study. The mean pain severity was 3.75 ± 2.25 and worst pain experienced was 5.73 ± 2.12 . The most common pain sites were: the knees (55.7%), wrist (43.5%), and neck (41.7%). Women experience higher prevalence of shoulder, upper back, and ankle pain ($P < 0.05$). In 62 cases (53.91%) MS interfered with daily functioning at least for a time. The prevalence of upper back and neck pain was higher in cases with a shorter disease duration ($P < 0.05$).

Conclusions: Pain was very common in patients with MS and not relevant to sex or age. In the majority of the cases more than 1 limb was involved and the prevalence of pain in the lower limbs was higher, especially in the knees. In females, the prevalence of pain in the shoulders, upper back, and ankle was higher compared to males. Also, neck and upper-back pain were found in the early stages of the disease.

Key words: Multiple sclerosis, Musculoskeletal pain, Pain measurement

Introduction

Multiple sclerosis (MS) is a chronic immune-mediated disease of the central nervous system that causes long-term physical disability (1). This disease is the most common non-traumatic cause of disability in young adults, affecting 350,000 individuals in the USA and millions worldwide (2,3). Throughout the course of the disease, pain is common and it is associated with many symptoms and problems (4). Studies have reported that 23% of patients had pain at the onset of

being diagnosed with MS and the prevalence of pain in MS ranged from 29% to 86% (5-7).

The mechanisms of pain in MS have not been identified (8). Several studies have shown that pain in MS patients can be caused by an inflammatory attack on fiber tracts or various sequels of MS such as extrapyramidal or cerebellar syndromes, bladder dysfunction, and limb paresis, leading to increased muscle tone with spasms, urinary tract infections, and postural abnormalities (8-11).

Corresponding Author: Mehran Fazli, Imam Khomeini Hospital of Esfarayen, Esfarayen Faculty of Medical Sciences, Esfarayen, Iran.

Email: mehnan222@gmail.com



THE ONLINE VERSION OF THIS ARTICLE
ABJS.MUMS.AC.IR

Table 1. Frequency (frequency percentage) of limb pain

Affected limbs	12 months preceding interview	7 days preceding interview	Interfering with daily functioning
Neck pain	48 (41.7%)	33 (28.7%)	18 (15.7%)
Shoulder pain	40 (34.8%)	29 (25.25)	19 (16.5%)
Elbow pain	31 (27%)	26 (22.6%)	21 (18.3%)
Wrist pain	50 (43.5%)	37 (32.2%)	27 (23.5%)
Upper back pain	38 (33%)	29 (25.2%)	19 (16.5%)
Backache	44 (38.3%)	35 (30.4%)	26 (22.6%)
Hip pain	43 (37.4%)	33 (28.7%)	25 (21.7%)
Knee pain	64 (55.7%)	51 (44.3%)	34 (29.6%)
Ankle pain	43 (37.4%)	40 (34.7%)	22 (19.1%)

Pain conditions associated with MS are classified into 4 major groups: continuous central neuropathic pain, intermittent central neuropathic pain, musculoskeletal pain, and mixed neuropathic and non-neuropathic pain, which have not been investigated thoroughly (8). Thus, this study aimed to investigate the severity and prevalence of musculoskeletal pain in MS patients in the Mazandaran Province (north of Iran) in 2013.

Methods

Study design and population

This cross sectional study's sample size requirement was based on Michalski et al.'s study and a considered of 5% error and 80% power was calculated for 115 patients (11). Members of the Mazandaran MS Association, who had an established diagnosis of MS, were randomly entered into this study. This study was a questionnaire based cross sectional study and patients participated with full awareness. However, we respected the privacy of the patients and assured them that their information would be held under legal obligations of confidentiality. Also, this research was approved by the ethical committee of the Mazandaran University of Medical Science.

Data collection

Data was collected by interviews and questionnaires. The Numeric Rating Scale questionnaire was used to measure pain severity (from 0 to 100). Thereby, 0 represents no pain and 100 the worst painful sensation. This questionnaire consists of 3 questions to explore the cases' current pain severity, highest rate of pain severity, and the average pain severity on the seventh

Table 2. Mean pain severity based on MS duration

Pain severity	Less than 2 years	More than 2 years	P value
At the time of study	3.66±2.22	4.07±2.34	0.11
Mean pain severity for disease duration	3.48±1.71	4.55±1.29	0.002
Mean of the worst pain	5.26±2.12	6.60±1.85	0.002

day preceding the interview.

The Nordic musculoskeletal questionnaire (NMQ-E) was used to investigate the cases of musculoskeletal pain. This questionnaire consisted of questions about the existence and duration of limb pain including neck, shoulders, elbow, wrist, upper back, back, hip, thigh, and knee (12).

Statistical analysis

The difference in percentages (qualitative variables) was analyzed using the X² test. Student's t-test was used to estimate standard deviation and the data was analyzed using SPSS version 16 software. A *P* value of <0.05 was considered statistically significant.

Results

Among the 115 participants with a mean age of 30.43±5.86 years (range: 18-52) 27 cases (23.5%) were male. In this study, the percentage of females to males was 3.25. The disease duration of 75 cases (65.2%) was less than 2 years and in 40 cases (34.8%) it was more than 2 years. The mean disease duration was 26.34±24.32 months (range: 7.5-200 months).

The frequency of musculoskeletal pain is shown in Table 1. According to these results, the most common limb pains were observed in the knee (55.7%), wrist (43.5%), and neck (41.7%). In the 12 months preceding the interview, 70 cases (60.9%) were suffering from chronic upper limb pain, 74 (64.3%) from lower limbs pain, and 53 (46.1%) from backache. In 62 cases (53.91%) musculoskeletal pain interfered with daily functioning at least for a time.

In terms of pain in the neck, wrist, back, hip, and knee, there was no significant difference between men and women (*P*>0.05). But 23.1% of men experienced

Table 3. Mean pain severity based on the sex of MS patients

Pain severity score	Males	Females	P value
At the time of study	3.33±1.75	3.63±2.50	0.55
Average pain severity	3.48±1.31	3.96±1.73	0.18
Mean of the worst pain	5.37±1.64	5.84±2.24	0.31

shoulder pain; 66.6% in the right shoulder, 16.7% in the left shoulder, and 16.7% in both shoulders. Also, 38.6% of women experienced shoulder pain; 17.64% in the right shoulder, 47.05% in the left shoulder, and 35.29% in both shoulders. Thus, a significant difference was observed between men and women in regards to shoulder pain ($P=0.043$). Upper back pain was experienced in 40.2% of women and 11.5% of men. Women had more back pain and the chance of upper back pain for women was 5.16 times more than men (OR: 5.16, & 95%, CI: 1.43-18.50, $P=0.007$). In addition, the prevalence of ankle pain was 45.5% in women and 22.2% in men. In women, the prevalence of ankle pain was significantly higher compared with men, and ankle pain in women was 2.19 times more than men (OR: 2.19, 95%, CI: 1.07-7.92, $P=0.031$).

The results showed that the mean disease duration for cases experiencing neck pain on the seventh day preceding the interview was significantly lower compared with others (17.69±9.1 vs. 31.98±29.82 months) ($P=0.035$). Also, the mean disease duration for patients with upper back pain was significantly lower compared with others (17.24±9.17 vs. 31.45±29.62 months) ($P=0.039$). But the mean disease duration for patients whose knee pain interfered with their daily functioning was significantly higher compared with others (44.00±39.17 vs. 20.78±14.79 months) ($P=0.001$). No statistically significant difference was observed between the mean disease duration and other limb pains ($P>0.05$).

According to the results of the Numeric Rating Scale questionnaire, the point of prevalence of pain in patients was 87.8% (101 patients). Also, mean pain severity was 3.75±2.25 at the time of this study; 3.33±1.75 for males and 3.63±2.50 for females ($P=0.55$). Mean pain severity was 3.66±2.22 for cases whose onset of MS was more than 2 years and 4.07±2.34 for those less than 2 years ($r: 0.13, P=0.11$). The average pain score was 3.85±1.65; 3.96±1.73 for females and 3.48±1.31 for males. For those whose onset of MS was under 2 years the average pain score was 3.48±1.71 and for those over 2 years it was 4.55±1.29. There was a significant correlation between mean pain severity and disease duration ($P=0.002, r: 0.25$). In fact, there was no statistically significant difference between females and males in the average pain score ($P=0.18$). Also, the patients were asked to rank their worst pain from 0 to 100. The mean of the worst pain was 5.73±2.12; 5.37±1.64 for males and 5.84±2.24 for females ($P=0.31$) (Table 2 and 3). The mean of the worst pain was 5.26±2.12 for the patients whose onset of MS was less than 2 years and 6.60±1.85 for those more than 2 years. A significant correlation was observed between disease duration and patients' worst pain ($r: 0.25, P=0.002$).

Discussion

Multiple sclerosis is a chronic demyelinating and progressive disease of the central nervous system. Its incidence rate is reported not needed 2.5 per 100,000 and its prevalence rate is 2.5 million cases worldwide (13-16). Approximately half of MS patients are affected

with pain and nearly three-quarters of patients report having had pain within the preceding month (8).

According to this study, the prevalence of pain was 87.8% and the prevalence of pain reported by Michalski et al. and Svendsen et al. was 81.6% and 79.4%, respectively, which is in concordance with our results (11,6). According to several other studies the prevalence of pain in MS ranges from 29 to 86 (8). It is reported that the difference between points of prevalence in the studies is due to differences in definitions of pain, type of pain, sample size, survey technique, and tools of data collection (17-21). According to the literature, pain interferes with MS patients' daily functioning and dramatically affects patients' quality of life (22, 23).

The risk factors reported to be associated with MS are age, disease duration, course of the disease, and physical disability of patients (21). In this study only disease duration significantly correlated with pain severity, but no significant correlation was observed between pain severity and age or sex. Similar to our study, some studies reported that only certain risk factors correlated with pain severity in MS patients, but others reported discrepant results (5, 22, 24-26). Solaro et al. conducted a study on pain severity of a large sample size of MS patients and reported that there was a significant correlation between pain severity and disease duration and age (5). They reported that females experienced more pain compared with males (24). This result was not in concordance with our study, but several studies similar to our study showed that males and females experienced almost the same pain severity (5, 25, 27-29).

Similar to several other studies, we applied the Numeric rating score questionnaire to evaluate patients' pain severity. In two studies, patients reported pain severity as mild (mean: 2.8), but 4 of them rated pain severity from 4.8 to 5.8, which was close to our results (6, 22, 27-30).

In MS patients, limb pains were classified as continuous central neuropathic and back pain as neuromuscular pain (31). Similar to our study, Svendsen et al. reported that several patients experienced more than one limb pain simultaneously. Also, they observed that the most commonly affected limbs were lower limbs (96%), back (70%), and upper limbs (52%) (23). Osterberg et al. reported that among the patients suffering from central pain, the point of prevalence of lower limb pain was 87% and upper limb pain was 31% (26). In this study the point of prevalence of lower limb pain and back pain was lower compared to the study of Osterberg et al., but still the point of prevalence of the lower limbs was higher compared with other limbs (26). In addition, the point of prevalence of pain in the shoulder, upper back, and ankle was higher in females compared with males. A significant result of this study was that the point of prevalence of neck and upper back pain was higher in MS patients with shorter disease duration. Neck pain of MS patients is represented according to Lhermitte's sign, which is defined as feeling a transmit short lasing pain in the back of the neck and lower back associated with neck movements. It is reported that the point

of prevalence of neck pain can be up to 40%. In most patients, the symptoms resolve over 4-6 weeks, but in some it may recur during MS exacerbations (8).

The results show that pain is a very common phenomenon in MS patients living in the Mazandaran province. Pain prevalence is not correlated with sex and age, but there is a significant correlation between pain incidence and disease duration. In most patients, more than one limb are affected with pain simultaneously. Also, the point of prevalence of lower limb pain is higher, especially knee pain. The prevalence of shoulder, upper back and ankle pain was higher in females compared with males. Moreover, the prevalence of upper back pain and neck pain was higher in MS patients with a shorter disease duration.

Acknowledgements

We are grateful for being allowed to access the official archives of the members of the Mazandaran MS Association and for their help in collecting the data.

Masoud ShayestehAzar MD
Mohammad Hossein Kariminasab MD
Majid Sajjadi Saravi MD
Department of Orthopedic Surgery, Imam Khomeini Hospital, Mazandaran University of Medical Sciences, Sari, Iran

Mahmoud Abedini MD
Department of Neurology, Bu Ali Teaching Hospital, Mazandaran University of Medical Sciences, Sari, Iran

Mehran Fazli MD
Imam Khomeini Hospital of Esfarayen, Esfarayen Faculty of Medical Sciences, Esfarayen, Iran

Seyyed Abbas Hashemi MD
Pedram Abdizadeh MD
Faculty of Medicine, Student Research Committee, Mazandaran University of Medical Sciences, Sari, Iran

References

1. Wingerchuk DM, Lucchinetti CF, Noseworthy JH. Multiple sclerosis: current pathophysiological concepts. *Lab Invest.* 2001;81(3):263-81.
2. Pittock SJ, McClelland RL, Mayr WT, Jorgensen NW, Weinshenker BG, Noseworthy J, et al. Clinical implications of benign multiple sclerosis: A 20-year population-based follow-up study. *Ann Neurol.* 2004; 56(2):303-6.
3. Buchanan R, Wang S, Tai-Seale M, Ju H. Analyses of the minimum data set: comparisons of nursing home residents with multiple sclerosis to other nursing home residents. *Mult Scler.* 2003;9(2):171-88.
4. Ehde DM, Osborne TL, Jensen MP. Chronic pain in persons with multiple sclerosis. *Phys Med Rehabil Clin N Am.* 2005;16(2):503-12.
5. Solaro C, Bricchetto G, Amato M, Cocco E, Colombo B, D'Aleo G, et al. The prevalence of pain in multiple sclerosis A multicenter cross-sectional study. *Neurology.* 2004;63(5):919-21.
6. Svendsen KB, Jensen TS, Overvad K, Hansen HJ, Koch-Henriksen N, Bach FW. Pain in patients with multiple sclerosis: a population-based study. *Arch Neurol.* 2003;60(8):1089-94.
7. Hirsh AT, Turner AP, Ehde DM, Haselkorn JK. Prevalence and impact of pain in multiple sclerosis: physical and psychologic contributors. *Arch Phys Med Rehabil.* 2009;90(4):646-51.
8. O'Connor AB, Schwid SR, Herrmann DN, Markman JD, Dworkin RH. Pain associated with multiple sclerosis: systematic review and proposed classification. *Pain.* 2008;137(1):96-111.
9. Kerns RD, Kassirer M, Otis J. Pain in multiple sclerosis: a biopsychosocial perspective. *J Rehabil Res Dev.* 2002;39(2):225-32.
10. Pöllmann W, Erasmus L-P, Feneberg W, Bergh FT, Straube A. Interferon beta but not glatiramer acetate therapy aggravates headaches in MS. *Neurology.* 2002;59(4):636-9.
11. Michalski D, Liebig S, Thomae E, Hinz A, Bergh FT. Pain in patients with multiple sclerosis: a complex assessment including quantitative and qualitative measurements provides for a disease-related biopsychosocial pain model. *J Pain Res.* 2011;4:219-25.
12. Dawson AP, Steele EJ, Hodges PW, Stewart S. Development and test-retest reliability of an extended version of the Nordic Musculoskeletal Questionnaire (NMQ-E): a screening instrument for musculoskeletal pain. *J Pain.* 2009;10(5):517-26.
13. Induruwa I, Constantinescu CS, Gran B. Fatigue in multiple sclerosis—A brief review. *J Neurol Sci.* 2012; 323(1-2):9-15.
14. Braley TJ, Chervin RD. Fatigue in multiple sclerosis: mechanisms, evaluation, and treatment. *Sleep.* 2010;33(8):1061-7.
15. Compston A, Coles A. Multiple sclerosis. *Lancet.* 2008;372(9648):1502-17.
16. Fazli M, Shayesteh-Azar M. Correlation between the fatigue with gender, age and disease duration in multiple sclerosis patients. *Int J Med Invest.* 2013;2(4):206-9.
17. Solaro C, Uccelli MM. Pharmacological management

- of pain in patients with multiple sclerosis. *Drugs*. 2010;70(10):1245-54.
18. Kenner M, Menon U, Elliott DG. Multiple sclerosis as a painful disease. *Int Rev Neurobiol*. 2007;79:303-21.
 19. Nurmikko TJ, Gupta S, MacIver K. Multiple sclerosis-related central pain disorders. *Curr Pain Headache Rep*. 2010;14(3):189-95.
 20. Österberg A, Boivie J. Central pain in multiple sclerosis—sensory abnormalities. *Eur J Pain*. 2010;14(1):104-10.
 21. Truini A, Barbanti P, Pozzilli C, Cruccu G. A mechanism-based classification of pain in multiple sclerosis. *J Neurol*. 2013;260(2):351-67.
 22. Kalia LV, OConnor PW. Severity of chronic pain and its relationship to quality of life in multiple sclerosis. *Mult Scler*. 2005;11(3):322-7.
 23. Svendsen KB, Jensen TS, Hansen HJ, Bach FW. Sensory function and quality of life in patients with multiple sclerosis and pain. *Pain*. 2005;114(3):473-81.
 24. Hadjimichael O, Kerns RD, Rizzo MA, Cutter G, Vollmer T. Persistent pain and uncomfortable sensations in persons with multiple sclerosis. *Pain*. 2007;127(1-2):35-41.
 25. Beiske A, Pedersen E, Czujko B, Myhr KM. Pain and sensory complaints in multiple sclerosis. *Eur J Neurol*. 2004;11(7):479-82.
 26. Österberg A, Boivie J, Thuomas KÅ. Central pain in multiple sclerosis—prevalence and clinical characteristics. *Eur J Pain*. 2005;9(5):531-42.
 27. Archibald C, McGrath P, Ritvo P, Fisk J, Bhan V, Maxner C, et al. Pain prevalence, severity and impact in a clinic sample of multiple sclerosis patients. *Pain*. 1994;58(1):89-93.
 28. Ehde DM, Gibbons LE, Chwastiak L, Bombardier CH, Sullivan MD, Kraft GH. Chronic pain in a large community sample of persons with multiple sclerosis. *Mult Scler*. 2003;9(6):605-11.
 29. Ehde D, Osborne T, Hanley M, Jensen M, Kraft G. The scope and nature of pain in persons with multiple sclerosis. *Mult Scler*. 2006;12(5):629-38.
 30. Warnell P. The pain experience of a multiple sclerosis population: a descriptive study. *Axone*. 1991;13(1):26-8.
 31. Bagnato F, Centonze D, Galgani S, Grasso MG, Haggiag S, Strano S. Painful and involuntary multiple sclerosis. *Expert Opin Pharmacother*. 2011;12(5):763-77.