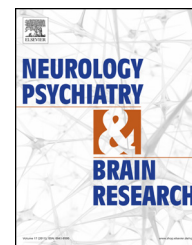


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# Beyond pain in multiple sclerosis



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## ABSTRACT

Although numerous studies had been performed to evaluate multiple sclerosis (MS) related pain, the exact cause of this syndrome is not clear. The aim of this study is to describe the prevalence and characteristics of pain in patients with MS, and to assess the associated clinical variables.

We consecutively collected data for 101 patients (74 women and 27 men; mean age,  $53.7 \pm 13.9$  years; mean EDSS,  $3.7 \pm 2.2$ ; mean duration of disease (years),  $13.6 \pm 9.7$ ).

Protocol variables were demographic (age, sex) and clinical (disease duration, disability, disease-modifying therapy, pain, sleep problems, fatigue, bladder/sexual dysfunction, depression and anxiety) data. Syndrome of pain manifested in 60.4% of participants and was significantly related with age, disease duration, disability, bladder/sexual dysfunction, depression and anxiety. Future research needs to dig into the mechanisms underlying the various MS-related pains to support mechanism-based approach to the treatment.

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## 1. Introduction

Multiple sclerosis (MS) is a demyelinating disease of the central nervous system, which affects different aspects of patients' lives. MS patients suffer from physical, emotional, cognitive, and social difficulties.<sup>1,2</sup> Pain is a common and complex experience for individuals who live with MS and it interferes with physical, psychological, and social function. Despite pain being a disabling symptom in patients with MS, its prevalence and characteristics are not quite established.<sup>3</sup> Pain, as a syndrome, is common in patients with MS. In MS literature the reported prevalence of pain ranges from 23 to 90 percent.<sup>4–6</sup> Although numerous studies have been performed to evaluate MS related pain, the exact cause of this syndrome is not clear. The aim of this study is to describe the prevalence

and characteristics of pain in patients with MS, and to assess the associated clinical variables.

## 2. Materials and methods

One hundred and one clinically definite relapsing-remitting (RR) MS patients (according to McDonald's criteria<sup>7</sup>) were enrolled in this study. The study was held at the Latvian Maritime Medicine Center. All patients signed their informed consent to undergo the procedure. The institutional review board approved the research.

Protocol variables were socio-demographic data (sex, age, residence, education, marital status, professional activity), MS clinical form (RR), disease duration, neurological dysfunction, defined according to the Expanded Disability Status Scale

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(EDSS), disease-modifying therapy (IFN beta or glatiramer acetate), pain, sleep problems, fatigue, bladder/sexual dysfunction, depression, and anxiety. All cases were examined by an expert neurologist to obtain Kurtzke EDSS.<sup>8</sup> Patients with active MS, an EDSS score of more than 6.5, cases under treatment of corticosteroids within the last 4 weeks, with severe medical comorbidities, drug and alcohol abuse, pregnancy, difficult mental conditions, pain-relieving drugs and nursing were excluded.

Patients were instructed to rate pain and bladder/sexual dysfunction intensity on an 10-point visual rating scale (VAS) ranging from 0 (no disturbance) to 10 (worst possible disturbance).<sup>9,10</sup> According to VAS, pain and bladder/sexual dysfunction were defined as severe (VAS 7–10), moderate (VAS 4–6), and mild (VAS 0–3). Coding of prevalence of pain and bladder/sexual dysfunction for further analysis was dichotomous – it was coded as present ( $\geq 4$ ) or absent ( $< 4$ ).

All participants were asked to fill in a Fatigue Severity Scale (FSS).<sup>11</sup> As recommended, we used a score of 4 or more in the FSS as a cut-off for the presence of fatigue.

Sleep problems were assessed using the 12-item Medical Outcomes Study Sleep (MOSS) scale.<sup>12</sup> A single indicator of mild, moderate, or severe sleep problems was calculated from item 12 of the MOSS scale based on the recommendations of Manocchia et al.<sup>13</sup> The sum of these scores was calculated as a total result (named sleep disturbances present/absent), and used in the further analysis.

Severity of depression and anxiety was evaluated using the Hospital Anxiety and Depression Scale (HADS) (HADS-A for anxiety and HADS-D for depression).<sup>14</sup> For further analysis we used the cut-point of  $> 10$  to define prevalent anxiety or depression.

All data was analyzed using SPSS software version 18.0.

Descriptive statistics, chi-square analysis, Student's t-test, ANOVA, Spearman and Pearson correlation, multiple linear regressions and odds ratios were calculated to describe the prevalence, difference, and likelihood of socio-demographic characteristics, clinical characteristics of RRMS, pain, fatigue, sleep problems, bladder/sexual dysfunction, depression, anxiety, and their comorbidity.

In the logistic regression analysis, the age, disease duration and EDSS variables were divided into 2 groups according to the median value.  $p$ -Value of  $< 0.05$  were considered to indicate statistical significance. All results are reported as mean  $\pm$  SD.

### 3. Results

We consecutively collected data for 101 patients (74 women and 27 men; mean age,  $53.7 \pm 13.9$  years; mean EDSS,  $3.7 \pm 2.2$ ; mean duration of disease (years),  $13.6 \pm 9.7$ ).

61 (60.4%) of the 101 patients studied endured pain. Sleep problems were reported by 55 (54.5%) patients. Fatigue was present in 57 (56.4%) study participants. In the sample of RRMS patients, 64 (63.4%) experienced bladder/sexual dysfunction. 34 (33.7%) of the 101 participants were clinically anxious, and 19 (18.8%) were depressive.

The prevalence of pain was significantly higher in older ( $p < 0.001$ ), with higher education ( $p < 0.001$ ), professionally not active, with longer disease duration ( $p < 0.001$ ), higher

EDSS score ( $p < 0.001$ ), absent disease modifying therapy ( $p < 0.01$ ), prevalent sleep problems ( $p < 0.05$ ), fatigue ( $p < 0.01$ ), bladder/sexual dysfunction ( $p < 0.001$ ), depressed ( $p < 0.01$ ) and anxious ( $p < 0.001$ ) patients. However, there was no statistically significant difference between patients' gender, residence, and marital status characteristics (Table 1).

The mean intensity of pain ( $p < 0.01$ ), disease duration ( $p < 0.001$ ), EDSS ( $p < 0.01$ ), sleep problems ( $p < 0.05$ ), bladder/sexual dysfunction ( $p < 0.01$ ), FSS ( $p < 0.01$ ), HADS-D ( $p < 0.05$ ) and HADS-A ( $p < 0.05$ ) scores were significantly different in different age groups (Table 2).

The survey did not find any significant differences comparing mean values of age, disease duration (years), EDSS score, and intensity of bladder/sexual dysfunction between genders ( $p > 0.05$ ). Male participants were more likely than females to have a higher mean score of fatigue (FSS,  $p < 0.05$ ) and anxiety (HADS-A,  $p < 0.001$ ). However, mean scores of pain

Table 1 – Characteristics of pain prevalence.

| Characteristics            | Total | Pain (%) | No pain (%) | $X^2$ | $p$ -Value |
|----------------------------|-------|----------|-------------|-------|------------|
| Gender                     |       |          |             |       |            |
| Female                     | 74    | 68.8     | 31.2        | 1.243 | $> 0.05$   |
| Male                       | 27    | 59.3     | 40.7        |       |            |
| Age (years)                |       |          |             |       |            |
| $< 50$                     | 64    | 46.9     | 53.1        | 4.476 | $< 0.001$  |
| $\geq 50$                  | 37    | 83.8     | 16.2        |       |            |
| Residence                  |       |          |             |       |            |
| Urban                      | 77    | 62.3     | 37.7        | 0.987 | $> 0.05$   |
| Rural                      | 24    | 54.2     | 45.8        |       |            |
| Education (years)          |       |          |             |       |            |
| $> 12$                     | 64    | 75.0     | 25.0        | 5.875 | $< 0.001$  |
| $\leq 12$                  | 37    | 35.1     | 64.9        |       |            |
| Marital status             |       |          |             |       |            |
| Not living alone           | 60    | 63.3     | 36.7        | 0.884 | $> 0.05$   |
| Living alone               | 41    | 56.1     | 43.9        |       |            |
| Professional activity      |       |          |             |       |            |
| Active                     | 23    | 30.4     | 69.6        | 5.523 | $< 0.001$  |
| Not active                 | 78    | 69.2     | 30.8        |       |            |
| Disease duration, years    |       |          |             |       |            |
| $< 10$                     | 77    | 50.6     | 49.4        | 6.375 | $< 0.001$  |
| $\geq 10$                  | 24    | 91.7     | 8.3         |       |            |
| EDSS                       |       |          |             |       |            |
| $< 4$                      | 56    | 42.9     | 57.1        | 6.463 | $< 0.001$  |
| $\geq 4$                   | 44    | 84.1     | 15.9        |       |            |
| Disease-modifying therapy  |       |          |             |       |            |
| Prevalent                  | 79    | 55.7     | 44.3        | 3.545 | $< 0.01$   |
| Absent                     | 22    | 77.3     | 22.7        |       |            |
| Sleep problems             |       |          |             |       |            |
| Prevalent                  | 55    | 69.1     | 30.9        | 1.225 | $< 0.05$   |
| Absent                     | 46    | 50.0     | 50.0        |       |            |
| FSS                        |       |          |             |       |            |
| Prevalent                  | 57    | 73.7     | 26.3        | 4.327 | $< 0.01$   |
| Absent                     | 44    | 43.2     | 56.8        |       |            |
| Bladder/sexual dysfunction |       |          |             |       |            |
| Prevalent                  | 64    | 79.7     | 20.3        | 8.222 | $< 0.001$  |
| Absent                     | 37    | 27.0     | 73.0        |       |            |
| Depression                 |       |          |             |       |            |
| Prevalent                  | 19    | 84.2     | 15.8        | 4.582 | $< 0.01$   |
| Absent                     | 82    | 54.9     | 45.1        |       |            |
| Anxiety                    |       |          |             |       |            |
| Prevalent                  | 34    | 88.2     | 11.8        | 6.894 | $< 0.001$  |
| Absent                     | 67    | 46.3     | 53.7        |       |            |

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