

**THE CORRELATION BETWEEN NEUROLOGICAL DEFICITS AND SUBJECTIVE EXPERIENCE OF ILLNESS IN MULTIPLE SCLEROSIS PATIENTS  
POVEZANOST NEUROLOŠKOG DEFICITA I DOŽIVLJAJA BOLESTI OBOLELIH OD MULTIPLE SKLEROZE**

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**Abstract:** *The present study compared neurological deficits and subjective experience of illness, i.e. quality*

*of life (QOL), in 60 persons suffering from multiple sclerosis. The functional status was assessed using the*

*Expanded Disability Status Scale (EDSS), the Paced Auditory Serial Addition Test (PASAT), the Beck De-*

*pression Inventory (BDI) and the Fatigue Severity Scale (FSS), whereas the subjective experience of illness*

*was evaluated using the general quality of life questionnaire SF-36 and the multiple sclerosis disease-specif-*

*ic quality of life questionnaire MSQOL-54. The study results showed that QOL was significantly impaired*

*in patients with more marked neurological deficits who suffered from depression and fatigue; the impact of*

*depression on the EDSS score was not statistically significant, whereas the impact of fatigue was.*

**Key Words:** *multiple sclerosis, quality of life*

**Sažetak:** *Da bi se uporedio neurološki deficit i doživljaj bolesti odnosno kvalitet života obolelih od mul-*

*tiple skleroze (MS) izvršeno je ispitivanje na uzorku od 60 ispitanika. Za procenu funkcionalnog statusa*

*korišteni su: Skala za procenu neurološkog deficita (Expanded Disability Status Scale - EDSS), Tempom*

*uslovljen auditivni test serijskog sabiranja (Paced Auditory Serial Additional Test - PASAT), Bekova skala*

*depresije (Beck Depression Inventory - BDI) i Skala težine zamora (Fatigue Severity Scale - FSS), dok su za*

*procenu doživljaja bolesti korišteni: opšti upitnik kvaliteta života tj. Upitnik o zdravstvenom stanju SF-36*

*i za bolest specifičan upitnik za procenu kvaliteta života MSQOL-54. Rezultati istraživanja ukazuju da je*

*kvalitet života značajno snižen kod obolelih sa izraženijim neurološkim deficitom i kod postojanja depre-*

*sivnosti i zamora; ne postoji statistički značajan uticaj depresivnosti na EDSS skor, dok je uticaj zamora*

*na EDSS skor statistički značajan*

**Ključne reči:** *multipla skleroza, kvalitet života*

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**INTRODUCTION**

The quality of life (QOL) in patients suffering from MS has been extensively investigated. On one

hand, McCabe and McKern (1) showed that both subjective and objective quality of life in patients with MS was significantly impaired compared to healthy population. Similar data was published by Nicholl et al. (2). On the other hand, Pittock et al. (3) concluded that 77% of the MS population was satisfied with their quality of life, despite developed physical impairment. The clinical course of the disease has proved to be an important factor in determining the quality of life. Janardhan and Bakahi (4) compared relapsing-remitting multiple sclerosis (RRMS) and secondary-progressive multiple sclerosis (SPMS) and came to a conclusion that the quality of life in patients with SPMS was substantially worse. The relation between the duration of the disease and the quality of life is a subject of much controversy. Myers et al. (5) reported that QOL in patients with MS improved in the course of illness, while others reached completely contradictory results. Dilorenzo et al. (6) concluded that the patient's age did not affect the QOL whereas depression and nervousness did. The loss of cognitive function has shown to be a solid indicator of lower QOL (7).

The lack of a uniform database that would allow monitoring of the health situation in MS patients has created a need for multidimensional research that would determine correlation between objective illness-related deficits and subjective perception of the patient. Therefore, further research is needed that would enable treatment and rehabilitation planning and psychosocial support for the patients and their family.

Rothwell et al. (8) concluded that vitality, general health and mental health were more important to MS patients than mobility deficiency, although physicians used to claim contrary. It is very important that MS patients are thoroughly interviewed, in addition to the neurological examination, in order to tease out possible sleeping disorders, mood/depression and fatigue. Only such a multidimensional concept can provide an adequate treatment and strategy for improvement of QOL in MS patients.

It has been established that health-related QOL can predict the course of the disease (9). However, a lot of MS patients with severe neurological deficits are very easily fatigued and consequently have poorer attention and concentration, which can limit the choice of the QOL questionnaires to be used. Additionally, the presence of emotional or cognitive problems in patients with MS may large-

ly affect their perception and ability to express adequately their current QOL (10).

## **OBJECTIVE**

The objectives of the research were:

Assessment of QOL and health status in MS patients using the MS disease-specific QOL questionnaire and the general QOL questionnaire

Assessment of the objective neurological status using appropriate measures

Evaluation of the effects of neurological deficits, depression and fatigue on QOL in MS patients

## **MATERIAL AND METHODS**

### **Study sample**

The study comprised a random sample of 60 people suffering from MS, irrespective of the form of the disease, of both sexes and of different professional orientation, who satisfied the following criteria: a multiple sclerosis diagnosis made according to McDonald criteria (11), age 18-56 years (12), EDSS score 0-6.5. Only patients that had been diagnosed at least six months before inclusion as to avoid the state of current crisis and clinically stable patients without exacerbations in the previous 30 days were included. Patients with severe cognitive dysfunction (ascertained through an interview and relevant medical records), patients with a history of substance abuse or psychiatric disorders and patients with sensory damage were excluded.

### **Methods**

The research instruments used included the general QOL questionnaire SF-36; MSQOL-54 for the assessment of QOL in MS patients; the Fatigue Se-

verity Scale (FSS) for the assessment of subjective experience of fatigue; the Beck Depression Inventory (BDI) for the assessment of depression; the Paced Auditory Serial Addition Test (PASAT) for the assessment of cognitive fatigue; and the Expanded Disability Status Scale (EDSS) for the evaluation of the functional status/neurological deficits.

### **Data processing and statistical methods**

The data obtained was coded and entered into a specially designed database. The data was processed using appropriate mathematical and statistical procedures in the SPSS version 11.5 and Statistica 6.0 programmes. The statistical methods

were chosen in accordance with the nature of variables tested, the research objective and the postulated hypotheses. The results were displayed in tables and figures.

## **RESULTS AND DISCUSSION**

The research included 60 out of approximately 1500 MS patients in Vojvodina, which makes 4% of the MS population. Subjects were selected randomly from among outpatients treated at the Clinic of Neurology of the Clinical Centre of Vojvodina. The ratio of men and women included in the study was 55% vs. 45%, indicating a similar presence of both sexes. The educational structure of the subjects was considerably better than that of the general population. Literature data on effects of the level of education on the evaluation of QOL in MS patients is scarce.

Somewhat surprisingly, only 3.3% of MS patients were divorced; as many as 63% were married, and 33% single, indicating that our subjects lived in relatively stable social environments, which was expected to have a positive effect on QOL. Likewise, 58.3% (35 subjects) had children, which is believed to provide a positive stability centre.

As regards employment, the study group was in a more favourable position in comparison with the general population in our country; only 16 subjects (26.7%) were unemployed, 41 (68.3%) had regular incomes, and 3 (5%) were students.

Results of previous studies dealing with factors associated with health-related QOL in MS patients have suggested that younger MS patients score better on physical examination tests and worse on mental examination tests (13-19).

It has been reported that MS patients with cognitive impairment have more difficulty finding a job, are more socially isolated and less active in everyday activities than patients with similar but exclusively physical impairment. MS patients are thus more concerned with their mental health, emotional problems and vitality than with their physical limitations. The causes of cognitive and emotional dysfunction in MS patients may be related to localisation and expansion of demyelination as well as to psychosocial consequences associated with the chronic disabling disease (20).

The final scores on the MSQOL-54 questionnaire for the whole sample showed that physical and mental health had a similar effect on QOL (63.75 vs. 67.03); yet physical impairment had a somewhat more pronounced negative effect on QOL

Combined score of physical health

Combined score of mental health

Physical function	64.22
Concern with own health	70.86
Perception of one's own health	53.46
Global quality of life	61.26
Energy/ fatigue	55.69
Emotional well-being	61.26
Role limitation- physical	49.57
Role limitation- emotional	71.26
Pain	71.72
Cognitive function	74.14
Sexual function	80.80
Social function	74.71
Concern with own health	70.86
Final score	63.75
Final score	67.03

*Table 1 - Average scores on MSQOL-54*

Regarding the physical health, in particular sexual functioning, the results obtained were surprising, with subjects rating highest their sexual functioning. This finding is unexpected considering the widely accepted opinion of medical workers that questions regarding sex are unwillingly discussed and commonly avoided on account of the popular belief that patients are considerably disabled due to physical or, even more, mental factors. Moreover, in previous studies there has been a high degree of unavailable data in MSQOL-54 sexual function scales. The unavailable data correlated with the degree of functional disability, and patients found the questions regarding their sexual activities too personal or irrelevant (They had not been involved in sexual relationships in the previous month). In addition, patients tend to avoid answering these questions in interviews (21). Physical role limitation, which is generally considered the most significant factor for impaired QOL, was not expected in the study group, for several reasons. Firstly, our subjects had a relatively

mild functional disability with low average EDSS scores (3.42 for men and 2.76 for women). Such a low physical limitation score is, however, contrary to the impression of a trained observer. As literature data suggests, it can be explained by a psychological mechanism of adjusting to the disease, where the patients adjust their (self) expectations, their functioning and their goals to the course and progress of the illness. If this widely accepted theory is valid, then it can be said that physical limitations are the least susceptible to rationalisation, due to strong correlations with assessment and objectification.

Similarly, the combined score of mental health showed that our patients assessed their cognitive function as a factor that has the least effect on their QOL. This finding may be explained by the fact that cognitive function is the most difficult to measure and the patients are not familiar with “cut-off values” for cognitive impairment. On one hand, analyses of the brain volumetric magnetic resonance imaging (MRI), measurements of the information processing speed, neurological testing of MS patients, have shown that cognitive deficits appear from the very onset of the illness, i.e. within the first two years in a majority (20-50%) of patients. On the other hand, if we do not want to question the patients’ evaluation, we can adopt the attitude that only a part of the entire cognitive potential is used in everyday activities and that changes in the brain volume of 0.3-1% are difficult to spot by a clinician during a routine clinical examination. In the early stages of MS, these changes are six times less frequently found than on neuropsychological tests. Therefore, a patient without specialised knowledge in this area and without criteria for evaluation is even less likely to be able to identify own cognitive impairments than a neurologist can do based on his or her clinical impression. Moreover, cognitive impairments in MS patients occur as sub-cortical dementia, representing a mild and gradual fall in overall functioning rather than a focal deficit affecting considerably one function only, which would be easier for the patient to identify.

*Table 2 – Average combined scores of physical health on MSQOL-54 according to the employment status*

COMBINED SCORE OF PHYSICAL HEALTH - FINAL SCORE

unem-  
ployed  
stu-  
dents  
em-

ployed  
retired  
Physical func-  
tion  
68.00  
61.67  
67.50  
52.92  
Perception of  
own health  
59.00  
56.67  
57.41  
42.31  
Energy / fatigue 63.20  
65.33  
54.52  
47.08  
Role limitation  
– physical  
50.00  
83.33  
52.77  
34.62  
Pain  
72.22  
66.67  
76.17  
63.08  
Sexual  
function  
87.05  
74.58  
80.02  
69.69  
Social  
function  
76.11  
75.00  
76.23  
69.87  
Concern with  
own health  
72.00  
63.33  
72.59  
56.92  
FINAL SCORE: 67.12  
67.76  
65.97  
52.97

failed to prove it with certainty, yet it can be assumed that students are the ones who are the least exposed to situations in which they can recognise inadequacy of their mental functions. In contrast, the retired patients had the overall lowest score of mental health, which is explained by the progression of their illness that rendered them unable to work. The youngest students had the best overall physical score which also implies the shortest duration of the disease. In contrast, the retired patients i.e. individuals with progressive illness had the lowest physical score (52.97 out of the maximum 100).

The average scores on the SF-36 indicate that the subjects assessed with the highest scores their general health condition, followed by social support and mental health. Impact of sight damage had the lowest score, which means that the subjects did not have sight problems that could affect their daily activities.

A Canadian study with 198 patients showed that MS had a drastic influence on patients' QOL. This was the most evident among patients with the lowest EDSS scores, or at the time when their walking difficulties were not a dominant symptom i.e. patients with lower EDSS had much better QOL than the ones with higher EDSS scores (20).

COMBINED SCORE OF MENTAL HEALTH - Final score

unemployed

stu-

dents

em-

ployed

retired

Concern

with own

health

72.00

68.33

72.59

56.92

Global

QOL

56.13

54.50

56.19

48.75

Emotional

well-being

72.80

68.00

69.04

64.92

Role

limitation -

emotional

86.67

77.78

66.67

61.54

Cognitive  
function

71.33

63.33

78.52

70.77

FINAL  
SCORE:

72.79

67.27

68.08

60.97

*Table 3 - Combined scores on MSQOL-54 mental  
health scales according to employment*

Scale

Num-  
ber of

par-  
tici-

pants

Low-

est

score

High-

est

score

Average SD

General  
health

58

22.67 100.00 79.5632 9.21779

Modi-  
fied im-

pact of

fatigue

scale

57

15.00 95.00

54.3966 20.07699

MOS

scale of

pain in-

fluence

57

28.00 50.00

35.1228 6.77988

Sexual

pleasure

56

18.00 83.00

40.7544 3.57711

Bladder

control

57

18.00 34.00

20.9298 4.47158

Bowel

control

57

18.00 30.00

19.9655 2.69480

Sight

damage

control

58

14.00 55.00  
 15.1964 6.77541  
 Impair-  
 ment  
 percep-  
 tion  
 58  
 21.00 100.00 45.8276 20.26243  
 Mental  
 health  
 ques-  
 tion-  
 naire  
 58  
 45.00 69.17  
 57.9885 5.06545  
 Modi-  
 fied  
 MOS  
 social  
 support  
 ques-  
 tion-  
 naire  
 58  
 20.00 95.83  
 78.5920 18.28223

Table 4 – Average scores on the SF-36 questionnaire

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Figure 1 – EDSS scores in males and females

EDSS  
 0-1.5  
 4.5-6.5  
 2-4  
 Count  
 50  
 40  
 30  
 20  
 10  
 0  
 Percent75  
 50  
 25  
 0  
 5  
 8  
 47

Figure 2 - EDSS score in men and women

With regard to neurological deficits, the vast majority of subjects had an EDSS score 2 - 4, indicating that it did not disturb their daily activities. Overall, men had a higher EDSS score (3.42) than women (2.76). In previous studies, EDSS score was correlated with numerous parameters although there is no literature data about the difference in the severity of the disease expressed as the EDSS score between men and women. Considering the slight overall differences in the EDSS scores in our study, they did not have significance and showed interrater and intrarater variations. However, EDSS score is one of the most important predictors of the treatment costs and rehabilitation of MS patients. All differences among treatments will depend on relapse rates and the progression of the disease in time (22).

Figure 3 – EDSS score according to work status  
 There was no statistically significant difference in the EDSS scores between employed and unemployed subjects. Retired subjects had the highest EDSS score, indicating the worst QOL. There was a discrepancy in the group of students, where we recorded high EDSS scores. Contrary to our results, a study by Miller et al. (23) from 2000 showed a significant association between the EDSS score and employment; in the group of patients with the EDSS score from 0-3, the percentage of the employed was 42%, part-time employees 20.5% and unemployed patients 37.5%. In the group where the EDSS score was from 3.5-6.5, the number of employed participants was 15.4%, part-time employees 10% and unemployed patients 17.4%.

*Table 5 - Average scores on the BDI*

GROUPS OF PARTICIPANTS

Number of subjects (%)

1

State without depression

22 (36.7)

2

Mild depressive state 19 (31.7)

3

Moderate depressive state

13 (21.7)

4

Severe depression

6 (10)

TOTAL

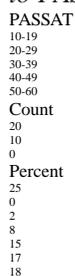
60 (100)

Most of the subjects in our study, 36.7%, did not suffer from depression, and only 10% had severe depression. There was a significantly larger number of women suffering from depression; out of 27 men from the total sample, only 37% suffered from depression (irrespective of its severity), whereas

reported in previous similar studies. The association between depression and the level of disability i.e. the neurological deficits, was confirmed in our and some other studies (25), but not in others (26). Depression represents an important predictor of both dimensions of QOL (physical and mental), irrespective of the neurological deficits (27). An important question, that yet needs to be answered, is whether depression impairs QOL, or the patients suffering from depression perceive themselves as sicker/more disabled than they truly are, which results in the findings just as the ones in our study, showing a correlation between the BDI and QOL.

When applying tests for the evaluation of the cognitive status, due to the cognitive fatigue MS patients may provide incorrect or incomplete information, and a large number of instruments/scales for measuring QOL have numerous questions that demand a substantial cognitive effort over a longer period of time.

*Figure 4 –Distribution of patients according to PASAT scores*



Literature data on pathognomonic, i.e. cut-off, values on the PASAT scale varies considerably. In our study, PASAT results were defined in the following way: a significant change (12-19 correct answers) was registered in 2 subjects, a mild change (20-39 correct answers) was registered in 23 subjects, whereas minimal impairment that did not affect routine daily activities (40-60 correct answers) was registered in 35 subjects (58.3%) (Figure 4). Our results are in accordance with the data of other authors who have detected cognitive deficiency in 40% of patients. On average, 25% of MS patients show impairment on this test (28). The level of impairment on the PASAT test indicates cognitive deficiency that is expressed as cognitive fatigue and attention and memory problems. Because of its demand and sensitivity, even relatively modest achievements on PASAT demand preserved cognitive capacities.

On the fatigue scale, an average score was 3.65 (range 1-7). The subjects were divided into 2 groups according to their test scores. The first

group consisted of subjects with average scores 1.0-3.9, and the other group consisted of subjects with average scores 4.0-7.0. Figure 5 shows that a larger number of subjects had more severe fatigue issues.

*Figure 5 –Distribution of subject according to fatigue scale scores*

53.3%  
46.7%  
4.7  
1-3.9

A significant correlation was found between summarized PASAT scores and BDI scores. The correlation was of low intensity and positive, meaning that the level of depression increased along with increased cognitive fatigue ( $p=0.05$ ).

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*Table 6 – Correlation between PASAT and BDI*

Sum BDI  
PASAT  
0.27

The Fatigue Severity Scale showed a negative correlation with physical health, sexual function, satisfaction with own sexual functioning and emotional well-being and a positive correlation with the physical role limitation and perception of own health.

The severity of fatigue and depression had significant effects on the QOL. Furthermore, interaction of these two factors, i.e. their joint effect, had significant impact on the QOL of our patients. In the analysis of variance, the independent variables were the fatigue and depression, and the dependant variable was the QOL of the participants.

In the following analysis of variance, the independent variables were the fatigue and depression, and the dependant variable was the EDSS score.

*Table 7 –Analysis of variance with the QOL as the dependent variable*

SS  
Degr. of  
MS  
F  
p  
Intercept  
104847.9  
1  
104847.9  
11799391.4  
.000  
DEPRESSION  
1423.250  
14  
101.661  
114.368  
.001

FATIGUE  
 4133.167  
 22  
 187.871  
 211.355  
 .000  
 DEPRESSION\* FATIGUE  
 90.750  
 1  
 90.750  
 102.094  
 .002  
 Error  
 2.667  
 3  
 .889

*Table 8 – Analysis of variance with the EDSS score as the dependant variable*

SS	Degree of	MS	F	p
<b>Intercept</b>				
<b>DEPRESSION</b>				
114.136	1	114.136	4.183	.041
114.136	29	3.936	.144	.713
913.087	1	913.087	1.154	.286
1.154	29	.040	.000	.959
.413	1	.413	.000	.959
<b>FATIGUE</b>				
1.216	2	.608	4.864	.028
1.216	12	.101	.028	.861
<b>DEPRESSION* FATIGUE</b>				
1.072	5	.214	1.715	.206
1.072	12	.089	.072	.812

Our results showed that there was no significant effect of depression on the EDSS score, whereas the effect of fatigue on the EDSS score was statistically significant. A joint effect of these two factors on the EDSS score was not proven to be statistically significant.

### **CONCLUSION**

The results of this study form the basis for further research of QOL in a larger number of MS patients. This study has demonstrated the need for a routine neurological testing of MS patients with a consistent and appropriate cognitive rehabilita-

tion, all with the aim of preserving and promoting cognitive status of MS patients. Finally, a well-planned multidisciplinary approach to their motor and social rehabilitation is needed.

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