Research Article

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The Impact of the COVID-19 Pandemic on Patients Diagnosed with Chronic Inflammatory Demyelinating Polyradiculoneuropathy – Three-Year Follow-Up

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Abstract

Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) is a neurological disorder characterized by autoimmune disruption of the peripheral nervous system, resulting in progressive weakness and sensory disturbance in the extremities. Following the COVID-19 pandemic, many illnesses demonstrated unpredictable progression due to infection with SARS-CoV-2. This study aimed to evaluate the impact of the pandemic on patients with CIDP over a three-year period. We conducted a prospective study on 11 adult CIDP patients, assessing muscle strength using the Medical Research Council (MRC) sum score, sensory symptoms and functional disability with the Inflammatory Neuropathy Cause and Treatment (INCAT) disability score and overall Quality of Life (QoL) through a numerical rating scale (0–100) supplemented by a COVID-19–specific questionnaire. Results showed that 55.1% of patients were concerned about the pandemic, primarily due to fears of relatives or friends being infected. Concerns regarding CIDP status included difficulties in drug availability, limited hospital access and possible worsening of clinical presentation due to comorbidities. QoL correlated with age (rho = −0.58, $p < 0.01$), MRC-SS at testing (rho = +0.44, $p < 0.05$) and INCAT disability score at testing (rho = −0.60, $p < 0.01$). Patients with greater fear of COVID-19 had significantly worse QoL compared to those with little or no fear (54.1 ± 16.9 *vs.* 70.3 ± 17.9, $p < 0.05$). Our findings suggest that the COVID-19 pandemic had a significant negative impact on patients with CIDP, with contributing factors including the direct effects of the virus, psychological distress and restrictive measures that worsened disease progression.

Keyword: COVID-19; CIDP; Psychological status; Pandemic; Stress

Introduction

The coronavirus disease (COVID-19) spread worldwide during 2020 and 2021, which caused great panic and anxiety due to its rapid transmission and severe clinical symptoms [1]. COVID-19 appears to be the largest pandemic of our time [2]. Pandemics are severe stressors to vulnerable groups and this highly contagious disease exerts considerable impacts on mental health [3,4]. In the face of extreme life-threatening tension and fear, people tend to show some anxiety-related behaviors [5]. Since the COVID-19 outbreak, the Serbian government has taken several public health interventions, such as isolation, quarantine and social distancing to control further transmission. Serbian media prioritized patient care, isolation and reducing person-to-person transmission by insisting on a "Stay-at-home stay at home period" while restricting social interaction [6]. Protective apparel and social isolation were used to reduce the risk of infection in previous pandemic outbreaks [7]. On the other hand, unethical media-related false information about COVID-19 is present worldwide, resulting in more emphasized stress related to the unknown illness of this pandemic [8]. In some previous cases, emotional distress was particularly neglected among those most severely affected by the pandemic, such as patients with some other chronic disease. There is very little information regarding patients with chronic autoimmune diseases and the impact of the pandemic on their psychological status.

Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) is an autoimmune disease, characterized by progressive or recurrent symmetric proximal and distal weakness, sensory dysfunction and absent or reduced tendon reflexes of all extremities, developing over at least two months [9]. CIDP can lead to many functional impairments of unpredictable duration, which may significantly affect patients' Quality of Life (QoL) even in normal circumstances [10]. Different factors besides physical disability, such as pain, fatigue, anxiety and depression, can affect the course and outcome of CIDP [11].

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Previous studies have reported high rates of anxiety, insomnia, depression and stress symptoms among some other neuromuscular disorders, such as myasthenia gravis or amyotrophic lateral sclerosis there is evidence of increased anxiety and depression during the COVID-19 pandemic [12,13]. The current study aimed to assess the influence of the COVID-19 pandemic on patients with CIDP during the three-year follow-up.

Materials and Methods

We performed a prospective study from July 2020 (in March 2020 the first COVID-19 cases were reported in Serbia) up to July 2023. Subjects who were called up to participate were patients with CIDP, who were regularly checked up and treated in Neurology Clinic University Clinical Centre Nis. Initially, 11 patients (from 12 registered and regularly followed in Neurology Clinic Nis at the time of the start of the research) answered our call. Only patients who fulfilled the EFNS/PNS diagnostic criteria were included [9]. Also, the diagnosis of CIDP variants was made according to the EFNS/PNS criteria [9]. Patients were tested at the beginning of the study, 12 months later and three years after initial testing.

We collected socio-demographic and clinical data including gender, age, duration of the disease, therapeutic modality for CIDP, as well as the presence of significant comorbidities. Concomitant therapy was also noted. The Medical Research Council (MRC) 0–5 point scale (0 without movement, 5 normal strength) was used to evaluate the muscle strength [14]. The MRC Sum Score (MRC-SS) ranges from 0 to 60 and it comprises the following muscle groups bilaterally: shoulder abductors, elbow flexors, wrist extensors, hip flexors, knee extensors and foot dorsal flexors. MRC-SS one year before the assessment and at the time of the assessment was collected. The degree of functional disability was measured using the Inflammatory Neuropathy Cause and Treatment scale (INCAT) [15]. From the medical records, the data of INCAT score at the time of diagnosis, at nadir (the worst INCAT score obtained during the disease course) and one year before the current assessment was derived. If the patient was diagnosed less than one year before testing, we collected MRC-SS and INCAT from January and February 2020, just before the epidemic started in Serbia. Patients were also asked how they were feeling compared to the time one year ago regarding their health. The Patients' Global Impression of Change (PGIC), a 3-point verbal scale, was used to assess patients' perception of this change (*i.e.,* 'feeling better', 'feeling same' or 'feeling worse') through time. Overall QoL was self-estimated by the patients on a Numerical Rating Scale (NRS) from 0-100. In addition, we used a Pittsburgh sleep quality index (PSQI) and Hamilton scales for the assessment of anxiety (HAM-A) and depression (HAMD). Questionnaires were assigned to patients only after carrying out a clinical examination and collecting epidemiological data.

PSQI questionnaire consists of 19 self-rated questions. Components of the questionnaire measure self-perceived quality, duration, latency, common efficacy of sleep and functionality during the day. These 19 questions are grouped into seven groups, each scored from 0-3. The obtained global PSQI score is from 0 to 21, where higher scores indicate lower QoS. A total score of more than 5 indicates poor QoS. It has been the most used QoS questionnaire so far, which was translated and standardized in the Serbian language [16].

HAM-D measures the intensity of depression and the values are interpreted as follows: 0-9 (without depression), 10-13 (mild depression), 14-17 (mild to moderate depression) and 18 or more (moderate to severe depression) [17]. HAM-A measures the intensity of anxiety, where the ultimate values below 17 indicate the absence or mild anxiety, values between 18-24 mild to moderate anxiety and values 25-30 moderate to severe anxiety [18].

The study was approved by the Ethical Board of the University Clinical Centre Nis. All procedures were performed following the Boards' guidelines and regulations. All participants provided written informed consent.

Data were statistically processed by the IBM SPSS statistical software (version 21) for the Windows operative system. The research results are presented in tabular and graphic form. P values of less than 0.05 were regarded as statistically significant. Numerical data were presented as percentage or mean ± Standard Deviation (SD). The normality of data was tested by the Kolmogorov–Smirnov test. For group comparisons, $\chi 2$ test, Mann–Whitney U test and Student t-test were used, as appropriate. Correlations were assessed using Spearman's correlation coefficient. Factors that significantly correlated with lower QoL in univariate analysis ($p<0.05$) were included in the multiple linear regression analysis (enter method). Stepwise criteria were as follows: Probability of F to enter variable was ≤0.05 and probability to remove variable ≥0.10. For all statistical tests, significant testing was two-sided, where alpha was set at 0.05 for statistical significance and at 0.01 for high statistical significance.

Results

The main socio-demographic and clinical features collected at the beginning of the study are presented in **Table 1**.

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Table1: Socio-demographic and clinical features of CIDP patients (N=29).

Feature	Value
Female gender - N (%)	6 (54.5)
Age (mean ± SD, years)	46.3±13.7
Disease duration (mean ± SD, months)	49.3±35.1
INCAT overall at diagnosis (mean ± SD)	3.7±1.5
INCAT overall at nadir (mean ± SD)	4.3±1.5
INCAT overall one year ago (mean ± SD)	2.9±1.5
INCAT overall at testing (mean ± SD)	2.4±1.9
MRC-SS one year ago (mean ± SD)	50.3±6.4
MRC-SS at testing (mean ± SD)	53.2±6.0
CIDP variant – N (%)	
Typical	7 (63.6)
Atypical	4 (36.4)
EFNS/PNS NCS criteria - N (%)	
Definite CIDP	8 (72.7)
Probable or possible CIDP	3 (27.3)
Other diseases - N (%) *	
Present	8 (72.7)
Absent	3 (27.3)
Therapy – N (%)	
IVIg	5 (45.4)
Oral corticosteroids	6 (54.6)
Other therapy for CIDP – N (%)	
Pregabalin	3 (27.3)
Vitamins	6 (54.6)
Alpha-lipoic acid	4 (36.4%)
Note: INCAT = the Inflammatory Neuropathy Cause and Treatment scale; MRC-SS = The Medical Research Council scale sum score; CIDP = Chronic inflammatory demyelinating polyradiculoneuropathy; NCS= nerve conduction study; IVIg =intravenous immunoglobulin; * other diseases in this cohort were diabetes mellitus, arterial hypertension, anemia	

Regarding the period one year ago (from the first testing point), changes in INCAT, MRC-SS and PGIC are presented in **Figure 1**. Chances in these scores during the time of the study are presented in **Figure 2**.

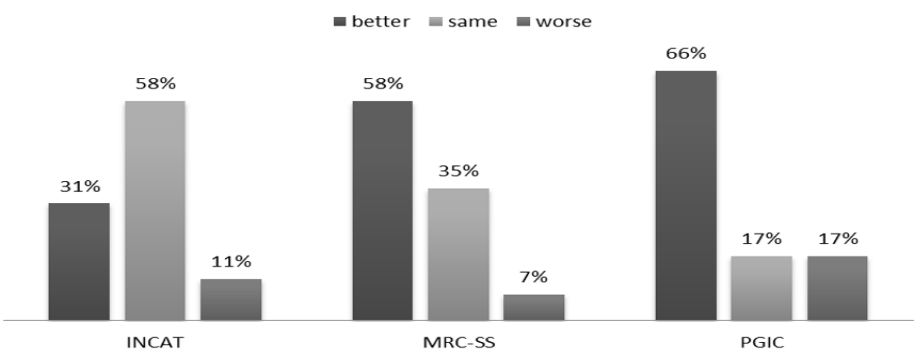

Figure1: Changes in INCAT, MRC-SS and PGIC regarding period one year ago from the first testing point.

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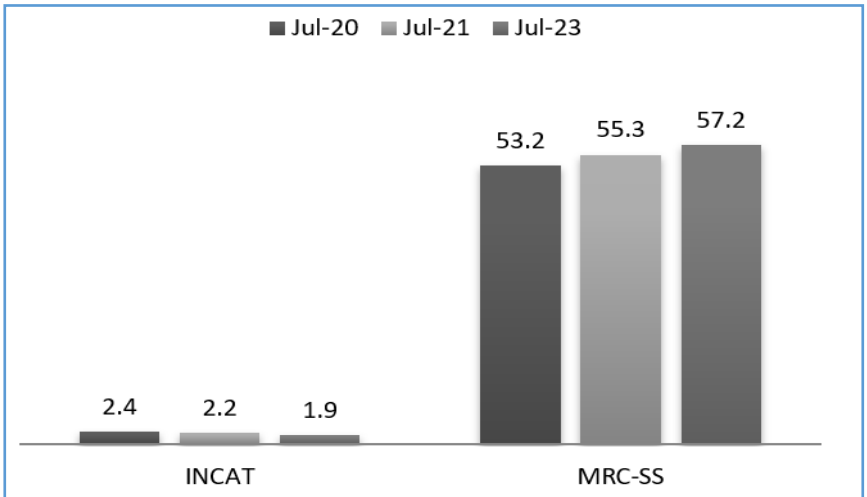

Figure 2: Values of INCAT score and MRC score during the course of the study.

Regarding the overall concern about the impact of the COVID-19 pandemic, we found that 55.1% of patients were concerned. The main reason for patients' concern was a fear that their relatives or friends could be infected with COVID-19. The daily activities of 65.4% of patients were negatively influenced by the pandemic. The main concerns about the CIDP status were that they would experience some difficulties in drug availability, that they could not go to the hospital as usual and that their clinical presentation would be worse because they have the concomitant disease. During the COVID-19 outbreak, 45.4% of patients reported their CIDP got worse. In 54.6% of CIDP patients, the pandemic influenced the therapy (reducing the dose or time interval or discontinuation due to the pandemic).

The test results for self-estimated QoL and PSQI, HAM-A and HAM-D during the time of the study are presented in **Table 2**. In our CIDP patients QoL was associated with patients' age (rho=-0.58, $p<0.01$), MRC-SS at the moment of testing (rho=+0.44, $p<0.05$) and INCAT disability score at the moment of testing (rho=-0.60, $p<0.01$). Patients with more fear of COVID-19 had worse QoL *vs.* those patients without fear or with mild fear (54.1±16.9 *vs.* 70.3 ± 17.9, $p<0.05$). All parameters that correlated with QoL in the univariate analyses were included in the multiple linear regression analysis (enter method). Independent predictors of worse QoL were age (beta=-0.35, $p<0.05$) and fear of COVID-19 (beta=-0.34, $p<0.05$). The overall model was significant with adjusted R2=0.53 ($p<0.01$).

Table 2: Scores on obtained tests during the course of the study (N -11).

Variables	July 2020	July 2021	July 2023
QoL (Mean ± SD)	66.3±18.1	65.2±17.0	73.2±12.0**
PSQI (Mean ± SD)	11.4± 3.5	11.6± 3.2	10.3± 3.2*
HAM-D (Mean ± SD)	10.2±6.2	11.0±5.6	8.4±5.6**
HAM-A (Mean ± SD)	9.4±7.3	9.6±6.7	8.6±6.3*
Note: $p<0.05$*, $p<0.01$**; SD = standard deviation; QoL – self estimated quality of life; PSQI = Pittsburgh sleep quality index; HAM-D = Hamilton depression scale; HAM-A = Hamilton anxiety scale			

Discussion

Our results suggest the high impact of the COVID-19 pandemic on the psychological status of patients with CIDP. People worldwide have different degrees of fear of COVID-19. In the study of psychological distress in the Chinese population during the COVID-19 outbreak, it was found that 35% of the general population experienced psychological distress [18,19]. By our results, it was reported that COVID-19 can specifically influence people with chronic diseases [20]. Studies in the Spanish and Turkish populations found that those with an accompanying chronic disease were psychologically the most affected by COVID-19 [21,22].

There are several possible reasons why CIDP patients may have pronounced psychological distress during the COVID-19 outbreak. First, it is still unknown

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if people with CIDP are at increased risk of developing severe clinical presentation of COVID-19 since they are a specific group, having immune-mediated disease and receiving immunomodulatory therapy [23]. There are case reports in the current literature that suggest potential exacerbation of disease symptoms due to SARS-CoV-2 in some CIDP and myasthenia gravis patients [24,25]. The study conducted on patients with another chronic disease (diabetes mellitus) showed that the main concern of these patients (in 56% of cases) was the fear of worse clinical presentation of COVID-19 if they become infected [26]. Another important issue is that it is not known if the CIDP disease course may be affected by SARS-CoV-2. Only a larger series of CIDP patients can show if SARS-CoV-2 may affect the disease course.

The COVID-19 pandemic has resulted in an unexpected opportunity to reexamine the need for immunomodulatory therapy in some CIDP patients. This therapy for CIDP patients is often continued by neurologists even if there is no need for that. In the PATH clinical trial, only 56% of CIDP patients treated with a placebo had CIDP relapse [27]. In the study conducted by Romozzi et al, over half of patients who stopped immunomodulatory therapy did not have to restart it [28]. Accordingly, no one of our patients in which discontinuation of chronic therapy was hastened due to the pandemic had disease worsening after more than five months of the follow-up. On the other hand, chronic immunoglobulin therapy may protect or reduce the risk of contracting infections, including COVID-19 so it can be useful for CIDP patients in these circumstances [29].

During the pandemic, check-ups should preferably be done by telemedicine or phone, but it is of note that telemedicine is neither widely available nor officially approved by the regulatory authorities in Serbia [30]. Subcutaneous immunoglobulin therapy, which could be self-administered as a home infusion, would be an adequate therapy solution [31,32].

Sleep disturbance is well recognized as a problem during the COVID-19 breakdown [33,34]. Worse sleep quality in the general population, measured before and during the pandemic, is noted in 5-10% of cases [35]. Also, more than 30% of the healthcare workers during COVID-19 reported worse sleep quality [36]. Pronounced sleep disturbances were noted in myasthenia gravis patients during the COVID-19 outbreak [10].

The impact of psychological factors on the well-being of CIDP patients during the COVID-19 pandemic is significant. Fear of COVID-19 was the strongest predictor of worse QoL in our cohort, even stronger than muscle weakness or functional disability. The study conducted on patients with cancer showed that 'being concerned about contracting coronavirus' was correlated with lower QoL [37]. Also, persons with a serious illness quarantined because of the increased risk of infections more often report symptoms of emotional disturbance, stress and depression [38]. For these reasons, professional psychological help and timely information are needed for chronic patients as soon as a health crisis starts.

There are several limitations of our study, such as a relatively small sample and possible intercultural differences so our results may not be easily extrapolated to other populations [39].

Conclusion

In conclusion, the COVID-19 pandemic has a significant impact on CIDP patients. Fear of COVID-19 was an independent predictor of lower QoL in CIDP patients during the pandemic. Besides the direct influence of the virus and fear of the virus, restrictive measures can indirectly harm patients with chronic diseases, such as CIDP.

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