Received: 29 August 2020 | Revised: 15 July 2021 | Accepted: 18 July 2021

DOI: 10.1002/mus.27378

CLINICAL RESEARCH ARTICLE

MUSCLE&NERVE WILEY

Impact of COVID-19 on the quality of life of patients with neuromuscular disorders in the Lombardy area, Italy

Delia Gagliardi MD[1,2] | Gianluca Costamagna MD[1,2] | Elena Abati MD[1,2] | Eleonora Mauri MD[2] | Roberta Brusa MD[2] | Luigia Scudeller MD[3] | Luca Andreoli MD[1] | Gaia Citterio MD[1] | Eleonora Piccin MD[1] | Francesca Magri MD[2] | Megi Meneri MD, PhD[2] | Daniele Velardo MD[2] | Monica Sciacco MD, PhD[4] | Nereo Bresolin MD[1,2] | Stefania Corti MD, PhD[1,2] | Giacomo Pietro Comi MD[1,2,4]

[1]Dino Ferrari Centre, Department of Pathophysiology and Transplantation (DEPT), Neuroscience Section, University of Milan, Milan, Italy

[2]Neurology Unit, IRCCS Foundation Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

[3]Scientific Direction, Clinical Trial Center, IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano Foundation, Milan, Italy

[4]Neuromuscular and Rare Diseases Unit, IRCCS Foundation Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

Correspondence
Stefania Corti, Dino Ferrari Centre, Department of Pathophysiology and Transplantation (DEPT), Neuroscience Section, University of Milan, Neurology Unit, IRCCS Foundation Ca' Granda Ospedale Maggiore Policlinico, Via Francesco Sforza 35, 20122 Milan, Italy.
Email: stefania.corti@unimi.it

Giacomo Pietro Comi, Dino Ferrari Centre, Department of Pathophysiology and Transplantation (DEPT), Neuroscience Section, University of Milan, Neurology Unit, Neuromuscular and Rare Diseases Unit, IRCCS Foundation Ca' Granda Ospedale Maggiore Policlinico, Via Francesco Sforza 35, 20122

Abstract

Introduction:/Aims: Patients with neuromuscular disorders (NMDs), including many elderly, immunosuppressed, and disabled individuals, may have been particularly affected during the coronavirus disease 2019 (COVID-19) pandemic in Lombardy, a COVID-19 high-incidence area between February and May 2020. We aimed to evaluate the effects of the COVID-19 pandemic on the quality of life (QoL) and perceived disease burden of this group of patients.

Methods: We conducted a cross-sectional phone-based survey study between June 1 and June 14, 2020, on a sample of 240 NMD patients followed at our clinic in Milan, Italy. We asked about perceived NMD burden and QoL before and during the COVID-19 pandemic. We collected responses on access to outpatient care and ancillary services. We investigated the presence of symptoms suggestive of COVID-19 infection and confirmed cases.

Results: We collected 205 responses: 53 patients (25.9%) reported a subjective worsening of the underlying NMD. QoL measures showed a significant worsening between pre and pandemic time frames (odds ratio, 2.14 95%; confidence interval, 1.82–2.51). Outpatient visits were postponed in more than half of cases (57.1%), with 104 patients (50.7%) experiencing a cancellation of scheduled diagnostic tests. 79 patients (38.5%) reported at least one symptom attributable to COVID-19 infection. Among the 10 patients tested with nasopharyngeal swabs, 6 tested positive and 3 died from respiratory failure, including 2 patients on corticosteroid/ immunosuppressive therapy.

Abbreviations: ADLs, activities of daily living; ALS, amyotrophic lateral sclerosis; CI, confidence interval; CIDP, chronic inflammatory demyelinating polyneuropathy; COVID-19, coronavirus disease 2019; IQR, interquartile range; MG, myasthenia gravis; MMN, multifocal motor neuropathy; MNDs, motor neuron diseases; MRC, Medical Research Council; NIV, non-invasive ventilation; NM, necrotizing myopathy; NMDs, neuromuscular disorders; OPMD, oculopharyngeal muscular dystrophy; OR, odds ratio; PEG, percutaneous endoscopic gastrostomy; QoL, quality of life; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Delia Gagliardi and Gianluca Costamagna contributed equally to the work.
Stefania Corti and Giacomo Pietro Comi contributed equally to the work.

Milan, Italy.
Email: giacomo.comi@unimi.it

Discussion: The COVID-19 pandemic affected QoL and limited access to outpatient care and ancillary services of NMD patients in Lombardy between February and May 2020.

KEYWORDS
access to care, COVID-19, immunosuppression, neuromuscular disorders, quality-of-life

1 | INTRODUCTION

Individuals with hereditary or acquired neuromuscular disorders (NMDs), including many elderly, immunosuppressed, and disabled patients, represent a concern for neurologists during the coronavirus disease 2019 (COVID-19) pandemic. In parallel, the crisis has forced the postponement of millions of visits and has prompted the rapid implementation of at-distance approaches. All these efforts have been critical to mitigating the burden of infection during the first phase of the pandemic, but they have had consequences on the quality of life (QoL) and well-being of patients who have been infected or have been required to practice strict preventative measures.[1-3]

Although some articles on NMD patients and their management during the COVID-19 pandemic have been published,[4-6] issues regarding this subgroup remain unsolved. (1) Some patients with NMDs may be at higher risk to develop a severe severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection due to the involvement of respiratory muscles and chronic use of immunosuppressive therapies,[7,8] but definitive data on infected NMD patients are still lacking.[9] (2) The health crisis has forced the dismantling of traditional health care services,[10] the postponement of in-person visits,[11] and the rapid implementation of at-distance approaches, but its impact at a population level is still unclear. (3) National authorities have imposed strict preventive measures, including prolonged home isolation, with uncertain consequences on the QoL of individuals with chronic debilitating diseases.

To answer these questions, we assessed the QoL and the burden of SARS-CoV-2 infection of NMDs patients followed up at our NMD Centre in Milan, Lombardy, one of the SARS-CoV-2 worst-hit regions worldwide.[12] Particularly, we aimed at evaluating whether and how the COVID-19 pandemic has affected patients' QoL and has had an impact on the provision of care following healthcare reorganization. Moreover, we have provided a detailed description of patients with a confirmed or suspected diagnosis of COVID-19, evaluating factors (eg, neuromuscular deficits, ongoing chronic treatment) potentially impacting the clinical course and the outcome of the infection.

2 | METHODS

We conducted a cross-sectional phone-based survey study between June 1 and June 14, 2020, among a sample of patients followed up at our NMD clinic in Milan, Italy. We included patients with consecutive sampling. Participants were both new and follow-up NMD patients who attended the clinic consecutively between February 1, 2019, and May 31, 2020. Inclusion criteria were: age 18 y or older and resident in Lombardy. Exclusion criteria included an undiagnosed NMD. All participants provided informed consent. Demographics were obtained from our institutional electronic records according to local regulations. The institutional review board of Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico approved the study. Patients were contacted between 9 am and 7 pm. Non-respondents were re-contacted up to three times within a week at different times of the day. In case of bedridden, tracheostomized, or severely cognitively impaired patients (five in total) caregivers were interviewed. All data used for analysis were aggregated to ensure patients' anonymity.

2.1 | Survey

The survey was divided into four sections (supplemental material):

1. Demographics and comorbidities: some data were retrieved from clinical records.
2. Perceived disease burden and QoL before the pandemic: improvement, stability or worsening of patients' perception of NMD compared to that before the pandemic (February 2020) was retrospectively assessed. Perceived QoL was assessed using a 5-point Likert-type scale focusing on six items: sleep, appetite, pain, mood, employment satisfaction, and social relationships. Likert-type scale grading ranged from 1 (low burden) to 5 (high burden).
3. Perceived disease burden and QoL during the pandemic: evaluation of subjective changes of NMD burden and QoL between February 20th (first SARS-CoV-2 confirmed case in Italy) and the day of the interview.
4. Suspected and confirmed COVID-19 cases: findings related to contacts with confirmed cases, presence of symptoms attributable to COVID-19, results of nasopharyngeal swabs, and serological testing were obtained. Management and outcome of confirmed cases were further investigated.

2.2 | Demographics

Age, sex, diagnosis, and disease duration were retrieved from the clinical records. Information on the use of immunosuppressants and steroid therapies were retrieved from the survey (question 10 to 13, supplemental material). Patients receiving oral steroids were on long-term therapy with low dose (≤7.5 mg prednisone equivalent a

day) and medium-dose (>7.5 mg, but ≤30 mg prednisone equivalent a day) corticosteroids.[13]

2.3 | Functional status

Patient functional status was assessed by asking about activities of daily living (ADLs) (bathing, personal hygiene, toileting, dressing, self-feeding, and transferring), respiratory support, presence of dysphagia, and ambulation (question 5 to 8, in the Supporting Information Material, which is available online).

2.4 | Statistical analysis

Mean ± SD are reported for continuous variables. Relative frequencies, percentages as well as medians with interquartile ranges (IQR) are presented for categorical variables.

To assess the effect of the pandemic period on perceived disease burden and QoL items, we employed multilevel mixed ordinal regression models, with "patient" as random effect and "timing" as fixed effect; these models take into account within-patient correlation and do not require further adjustment of *p*-value. We fitted a cumulative model of items, thus estimating a common effect of the pandemic on perceived disease burden and on the underlying trait "QoL," and a model with timing interacting with individual items, to assess whether the pandemic had a different effect on some of the individual QoL items. The reference timing was February 2020. To explore potential differences in subgroups, further models were fitted adding an interaction term between timing and each subgroup. The association of clinical features (age, sex, disease duration, independent ambulation, respiratory support, dysphagia, inflammatory disease, and steroid and immunosuppressive therapy) with changes in perceived disease burden and QoL during the pandemic period was also assessed.

Statistical analyses were performed using GraphPad (Prism) version 8.3.1 and STATA version 16.0 (Stata Corporation, College Station, Texas, USA).

3 | RESULTS

We contacted 240 out of 350 patients followed at our neuromuscular center and received 205 phone responses, resulting in a response rate of 85%; 110 undiagnosed patients under investigation for a possible NMD condition were excluded from the survey. Three patients out of 205 had died from COVID-19 infection, and 1 patient was unable to perform the survey due to a language barrier, resulting in 201 complete responses.

3.1 | Demographic and clinical features

Our sample consisted of eight subgroups of NMDs, including myositis (dermatomyositis, necrotizing myositis [NM], polymyositis, inclusion body myositis, and overlap myositis with rheumatoid arthritis) myasthenia gravis (MG), metabolic myopathies, muscular dystrophies, congenital myopathies, motor neuron disorders (MNDs), immune-mediated neuropathies (chronic inflammatory demyelinating polyneuropathy [CIDP], multifocal motor neuropathy [MMN], and anti-MAG neuropathies), and other neuropathies (diabetic, toxic, and hereditary).

The mean age of respondents was 61.7 ± 16.2 y (range 21–90). Male and female sexes were equally distributed, except for congenital myopathies, immune-mediated neuropathies, and MNDs. Demographic and clinical features are listed in Table 1. Comorbidities and functional disease status (dependence in ADLs, respiratory support, dysphagia, ambulation) are summarized in Supporting Information Table SS1. Hypertension and obesity-related comorbidities were the most represented.

Almost half of the patients were on maintenance therapy with corticosteroid or immunosuppressive drugs including patients with myositis, MG, and immune-mediated neuropathies (Table 1). Approximately 10% of patients were taking both steroids and immunosuppressive drugs.

3.2 | Perceived disease burden and QoL before and during the pandemic

3.2.1 | Perceived disease burden

Perceived disease burden was derived from questions 14, 15, and 22 (Supporting Information Material); 71.2% of patients did not experience any changes concerning their NMD during the COVID-19 pandemic, while 25.9% reported a subjective worsening of the disease burden. Perceived disease burden showed a significant worsening between February 2019 and May 2020 (odds ratio [OR] 3.75; 95% confidence interval [CI], 2.29–6.13, $p < .001$). No significant change was observed during the COVID-19 pandemic between February 2020 and May 2020 (OR 1.42; 95% CI 0.89–2.26; $P = .140$). Independent ambulation, inflammatory disease (myositis, MG, and immune-mediated neuropathies), and steroid therapy were associated with perceived disease burden worsening during the pandemic (Table 2). In the same timeframe, respiratory support and dysphagia were inversely associated with subjective worsening of NMD burden.

Taking into account the different NMD categories, perceived disease burden was significantly worsened in patients with metabolic myopathies, muscular dystrophies, and MNDs compared to myositis (Table 2).

3.2.2 | QoL

QoL item scores collectively significantly worsened between pre-pandemic (February 2020) and pandemic (May 2020) timeframes (OR 2.14; 95% CI, 1.82–2.51; $P < .001$). When analyzing QoL item scores individually, we found a statistically significant risk of

TABLE 1 Demographic and clinical features of patients with neuromuscular disorders

	Total (n = 205)	Myositis (n = 44–21.5%)	Myasthenia gravis (n = 44–21.5%)	Metabolic myopathies (n = 24–11.7%)	Muscular dystrophies (n = 27–13.2%)	Congenital myopathies (3–1.4%)	MNDs (n = 30–14.6%)	Immune-mediated neuropathies (n = 9–4.4%)	Other neuropathies (n = 24–11.7%)
Age, y (mean ± SD)	61.7 ± 16.2	62.2 ± 16.1	68.4 ± 14.3	55.8 ± 16.6	50 ± 14.7	57 ± 19.7	66.1 ± 10.2	65.3 ± 16.2	61.1 ± 19.2
Sex, n (%)									
Female	103 (50.2)	29 (65.9)	23 (52.3)	12 (50)	10 (37)	3 (100)	12 (40)	6 (66.7)	8 (33.3)
Disease duration, y (mean ± SD)	11.4 ± 11.6	7.8 ± 7	9.5 ± 8.9	18 ± 13.2	14.4 ± 13.1	31 ± 15.1	4.7 ± 3.6	12.9 ± 10.4	17.1 ± 17
Steroid therapy, n (%)									
Medium dose	23 (11.2)	11 (25)	8 (18.2)	-	-	-	1 (3.3)	2 (22.2)	1 (4.2)
Low dose	33 (16.1)	15 (34.1)	14 (31.8)	-	-	-	-	2 (22.2)	2 (8.3)
Immunosuppressants, n (%)	34 (16.6)	22 (50)	9 (20.4)	-	1 (3.7)	-	-	2 (22.2)	-
Steroid + immunosuppressant, n (%)	20 (9.8)	13 (29.5)	5 (11.4)	-	-	-	-	2 (22.2)	-

Note: Immune-mediated neuropathies included 5 CIDP, 2 MMN, and 2 anti-MAG neuropathies. Myositis included 7 dermatomyositis, 15 necrotizing myositis, 12 polymyositis, 8 inclusion body myositis, and 2 overlap myositis with rheumatoid arthritis.

TABLE 2 Association between perceived disease burden during pandemic period and clinical features

Reference = February 2020	Univariable	
Covariates	**OR [95%CI]**	***P*-value**
Age (ref = average age)	0.99 [0.96–1.02]	.391
Female sex (ref = F)	1.37 [0.54–3.46]	.502
Disease duration (ref = 1 y)	1.00 [0.96–1.04]	.931
Independent ambulation (ref = no)	3.80 [1–43-10.08]	**.007**
Respiratory support (ref = no)	0.08 [0.02–0.38]	**.002**
Dysphagia (ref = no)	0.21 [0.07–0.62]	**.004**
Inflammatory disease (ref = no)	16.43 [5.91–45.66]	**<.001**
Steroid therapy (ref = no)	14.08 [4.36–45.52]	**<.001**
Immunosuppressive therapy (ref = no)	1.23 [0.33–4.59]	.761
NMD subgroup (ref = myositis)		
Myasthenia gravis	0.95 [0.20–4.55]	.949
Metabolic myopathies	0.06 [0.01–0.43]	**.005**
Muscular dystrophies	0.04 [0.01–0.24]	**<.001**
Congenital myopathies	0.11 [0.00–4.55]	.248
MNDs	0.03 [0.01–0.15]	**<.001**
Immune-mediated neuropathies	0.95 [0.07–13.42]	.971
Other neuropathies	0.19 [0.03–1.14]	.070

Note: Bold values indicate significant *p*-values ($p < 0.05$)

worsening for employment satisfaction and social relationships (Table 3). No significant differences were found considering the various NMD subgroups (Table 4). Age, sex, disease duration, independent ambulation, respiratory support, steroid, and immunosuppressive therapy did not significantly modify the impact on QoL (Table 4), while having an inflammatory disease was directly associated with QoL worsening during the COVID-19 pandemic.

Relative frequencies of responses for each QoL item are reported in Figure 1. Medians and IQR of pre-and post-pandemic scores for each NMD subgroup are reported in Supporting Information Table SS2.

3.3 | Outpatient caring, ancillary services, and physiotherapy

The COVID-19 outbreak may have affected outpatient care and ancillary services, favoring at-distance approaches. We asked our patients about the delay or cancellation of on-site visits and diagnostic tests. Outpatient clinical visits were postponed in 117 cases (57.1%), while telemedicine visits were scheduled in only 9 cases (4.4%). Consistent with this, 104 patients (50.7%) could not undergo their scheduled diagnostic tests due to the COVID-19 emergency.

Of 205 patients, 87 (42.4%) were regularly performing physical therapy before the onset of the COVID-19 epidemic; 66 of them (75.9%) experienced a suspension or a frequency reduction of these sessions between February and May; 22 out of 66 patients (33.3%) reported a subjective worsening of the underlying NMD during the pandemic period.

TABLE 3 QoL items between pre- and post-pandemic timeframes

QoL items	OR [95%CI]	*P*value
February 2020		
Baseline *(ref = appetite)*	1.00	
Pain	1.89 [1.27–2.83]	.002
Work	2.96 [1.75–5.01]	**<.001**
Social relationships	1.63 [1.10–2.41]	.015
Sleep	3.90 [2.64–5.76]	**<.001**
Mood	3.89 [2.65–5.72]	**<.001**
May 2020		
Appetite *(ref = Feb 2020)*	1.54 [1.04–2.30]	.033
May 2020		
Pain	0.80 [0.46–1.40]	.430
Work	4.42 [2.14–9.10]	**<.001**
Social relationships	4.35 [2.52–7.52]	**<.001**
Sleep	0.94 [0.55–1.61]	.816
Mood	1.33 [0.78–2.27]	.289

Notes: The odds ratios refer to the probability of a 1 unit decrease of each item score (and 1 unit increase of pain score) compared to appetite at February 2020 (top), of appetite at May 2020 compared to February 2020 (mid), and of each item score compared to the change in appetite from February to May 2020 (bottom). Bold values indicate significant *p*-values ($p < 0.05$)

TABLE 4 Association between QoL item scores (cumulative trait) during the pandemic period and clinical features

Covariates	Univariable OR [95%CI]	*P*-value
Age (ref = average age)	1.00 [0.99–1.01]	.510
Female sex (ref = F)	0.85 [0.62–1.17]	.321
Disease duration (ref = 1 y)	1.00 [0.98–1.01]	.801
Independent ambulation (ref = no)	1.34 [0.95–1.88]	.095
Respiratory support (ref = no)	0.69 [0.40–1.18]	.177
Dysphagia (ref = no)	0.80 [0.55–1.15]	.229
Inflammatory disease (ref = no)	1.49 [1.08–2.05]	**.014**
Steroid therapy (ref = no)	1.42 [0.99–2.03]	.059
Immunosuppressive therapy (ref = no)	1.32 [0.85–2.06]	.212
NMD subgroup (ref = myositis)		
Myasthenia gravis	1.09 [0.67–1.79]	.728
Metabolic myopathies	0.61 [0.43–1.09]	.094
Muscular dystrophies	0.65 [0.37–1.15]	.138
Congenital myopathies	2.23 [0.63–7.81]	.212
MNDs	0.73 [0.43–1.24]	.244
Immune-mediated neuropathies	1.70 [0.75–3.83]	.201
Other neuropathies	0.91 [0.52–1.59]	.734

Note: Bold values indicate significant *p*-values ($p < 0.05$)

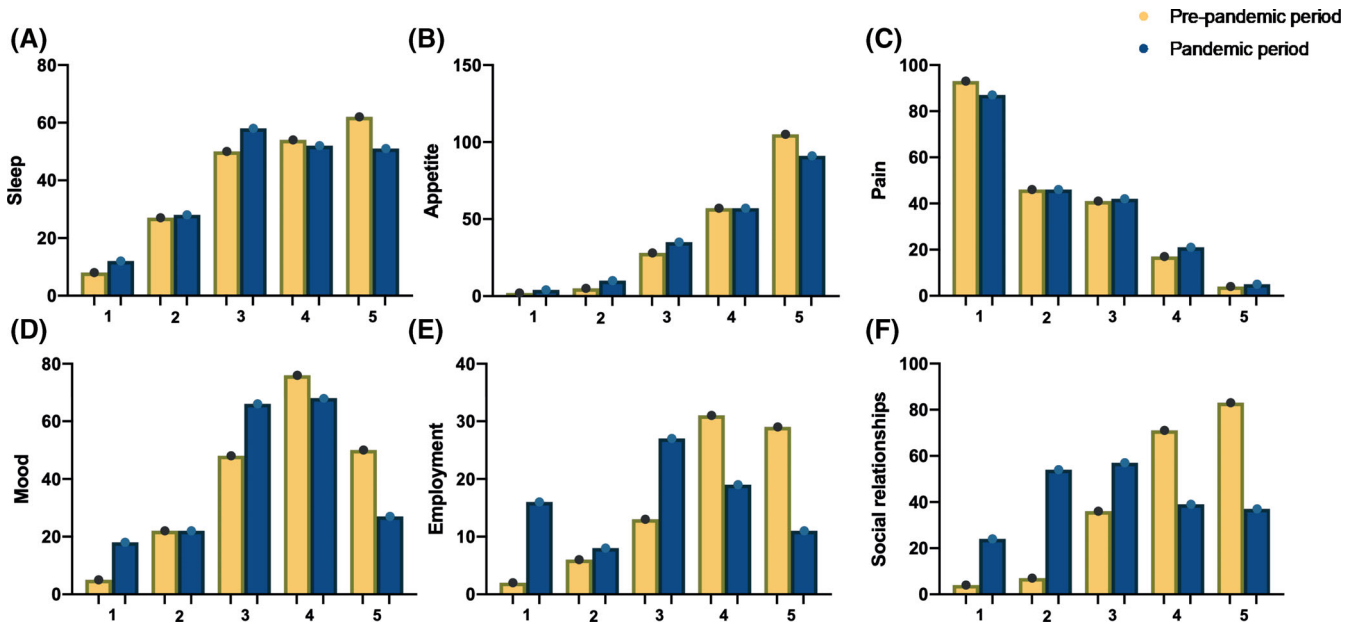

FIGURE 1 QoL changes before and during the COVID-19 pandemic. As regards the quality of life, sleep (A), appetite (B), pain (C), mood (D), employment (E), and social relationships (F) were ranked on a 1- to 5-point Likert-type scale. The histograms represent the frequencies of patients according to the score assigned to each item. Yellow columns, rates during the pre-pandemic period; blue columns, rates during the pandemic period

TABLE 5 Patients with confirmed COVID-19 infection

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Diagnosis	AChR-Ab MG	AChR-Ab MG	CIDP	OPMD	SRP-Ab NM	BMD
Age, y	88	61	50	80	85	32
Sex	Male	Male	Female	Male	Female	Male
Disease duration, y	8	1	26	9	0.5	12
Comorbidities	Hypertension, previous stroke	-	Hypertension, obesity/ dyslipidemia	-	Hypertension, obesity/ dyslipidemia	-
Baseline respiratory impairment	No	No	No	No	Yes	No
Prednisone, mg	2.5	17.5	-	-	75	-
Immunosuppressant	-	Azathioprine 150 mg daily	-	-	Rituximab 1 g (last infusion 1.5 mo before the infection)	-
Chest X-ray findings	Pneumonia	Not done	Interstitial pneumonia	Focal opacity + lung interstitial thickening	Multifocal interstitial pneumonia, pleural effusion	Unremarkable
Hospital admission	Yes	No	No	Yes	Yes	No
Therapy for COVID-19	Not available	Paracetamol	HQC, LMWH, azithromycin	Paracetamol, levofloxacin	HQC, antiviral (lopinavir/ ritonavir), Vancomycin	Paracetamol
Respiratory support	NIV	No	No	Oxygen therapy	NIV	No
Outcome	Death from respiratory failure	Full recovery	Full recovery	Death from respiratory failure	Death from respiratory failure	Full recovery

Abbreviations: Ab, antibodies; AChR, acetylcholine receptor; BMD, Becker muscular distrophy; HQC, hydroxychloroquine; LMWH, low molecular weight heparin; SRP, signal recognition particle.

3.4 | Patients with symptoms attributable to suspected or definite COVID-19 infection

Overall, 79 patients (38.5%) reported at least one symptom potentially suggestive of COVID-19 infection between February and the end of May. In our cohort, a total of 10 nasopharyngeal swabs were administered. Only eight (10%) of the symptomatic patients received a nasopharyngeal swab, with positive results confirmed by two repeated tests in six patients.

Considering confirmed cases (Table 5), all patients presented typical symptoms of COVID-19. Three out of six patients were hospitalized. They all showed signs of hypoxemic respiratory failure secondary to SARS-CoV-2 and received respiratory support. Patient 1 was on low-dose corticosteroid maintenance therapy. Patient 5 was on medium-dose corticosteroid therapy (30 mg), and she had received an infusion of rituximab, 1 g, 1.5 mo before. During the infection, patient 2 received a higher dose of steroids (from 17.5 to 25 mg daily) while maintaining azathioprine. All the hospitalized patients died due to respiratory failure.

Patients 2 and 3 reported a subjective worsening of neuromuscular symptoms following recovery from the infection, with increased fatigability and worsened distal weakness, respectively.

4 | DISCUSSION

Based on our survey, we found that the SARS-CoV-2 pandemic in Italy had an overall negative impact on access to visits, ancillary services, and QoL of our NMD patients regarding social relationships, mood, employment satisfaction, sleep, appetite, and pain.

As regards QoL, we observed a worsening in all the items evaluated in our survey. Different studies have assessed the QoL of residents in COVID-19 worst-hit areas,[14] patients with neurological diseases,[1,15] and individuals with suspected COVID-19 infection.[2] In all these studies, the pandemic had an overall negative impact on the QoL of the respondents. For instance, among 40 patients with Alzheimer disease in Spain, 30% of them reported a worsening of their health status during a 5-wk lockdown period.[1] Also in low-risk areas, the COVID-19 pandemic affected physical activity and QoL during the first wave, as reported in a study on NMD patients in Sicily.[15] In our cohort, employment satisfaction and social relationships were particularly affected. The fact that our patients come from Lombardy, where authority-appointed isolation measures were stricter compared with other parts of Italy, may have played a role. We did not observe significant differences in terms of QoL worsening among the various NMD subgroups, likely due to the heterogeneous and relatively small sample of patients and the short follow-up.

In our cohort, the perceived disease burden did not significantly change during the pandemic outbreak. However, patients with an inflammatory NMD and taking corticosteroids presented an increased risk of perceived disease burden worsening. Decreased access to outpatient care and in-person therapy adjustments may have affected patients' perception of their disease burden. Respiratory support, dysphagia, and dependent ambulation were associated with reduced perceived disease burden. It could be speculated that patients with more disabling NMDs, such as amyotrophic lateral sclerosis (ALS), may show disease-related behavioural changes, including apathy and lower awareness of clinical worsening,[16,17] possibly leading to bias in self-rating.

The literature on the clinical course of NMD patients with COVID-19 infection is scant. A small case series of five patients with MG and COVID-19 showed high variability of disease severity and outcome.[4] Three of them developed severe respiratory failure following the infection and required intubation or high-flow oxygen, whereas two had a milder disease course. Four of them had a favorable outcome. A patient with MG (patient 1) required non-invasive ventilation (NIV) during hospitalization and eventually died from respiratory failure. Patient 1 did not present with previous respiratory involvement. However, older age (88 y), a predictor of mortality in COVID-19,[18] may have played a role in this case. In some MG patients, COVID-19 may directly induce a myasthenic crisis.[5,19] Although an exacerbation of the underlying disease cannot be excluded in patient 1, our MG patient who recovered from the infection (patient 2) had milder symptoms and did not experience a flare of the underlying disease.

The fatal outcome observed in patient 4, who suffered from oculopharyngeal muscular dystrophy (OPMD), was likely due to respiratory impairment and old age.

Referring to immunosuppressive therapies, the need for therapy dosage reduction vs. discontinuation in NMD patients is uncertain[7] and large systematic studies on the outcome of infected immunosuppressed patients still lack. Preliminary systematic reviews do not report a significantly increased mortality or risk for a severe disease course in immunosuppressed patients with COVID-19.[9,20] Our cohort includes a limited number of patients with inflammatory diseases (44 inflammatory myositis and 9 immune-mediated neuropathies) from which to draw conclusions on the impact of immunosuppression in infected NMD patients. The need for discontinuing immunosuppressive therapy during COVID-19 infection for NMD will require further clinical studies.

It is still unclear how the isolation measures have affected the QoL of patients in different regions worldwide, particularly for those with chronic debilitating diseases. In addition, how the underlying NMDs and immunosuppression affect the COVID-19 disease course remains unanswered. On the other hand, it is essential to assess whether COVID-19 infection may prompt exacerbation of the underlying NMD in these patients. Studies investigating both pathogenic mechanisms of COVID-19 infection and comprehensive systematic analysis involving large cohorts will help to clarify these questions.

This study has limitations. Despite a satisfactory response rate (85%), our survey reached only a fraction of our patients. Symptoms and medical conditions were self-reported and likely limited by the availability of home thermometers as well as patients' recall and literacy. Since at the planning stage we could not anticipate the number of patients we would be able to enroll, we did not perform sample size calculations. The study size was based on patients' availability to

participate; our results should be viewed as exploratory and hypothesis-generating, rather than confirmatory. The use of an unvalidated Likert scale represents another limitation. Further, reported clinical worsening lacked an objective assessment using standardized scales (e.g. Medical Research Council [MRC] scale for muscle; 6-minute walk test; five times sit to stand test). However, surveys are a simple and quick tool to reach people at distance and have been used to assess QoL and disease burden of NMD patients in the past.[21,22]

With our survey, we showed that the COVID-19 pandemic impaired some aspects of QoL and affected access to outpatient care and ancillary services, with limited use of at-distance alternatives, of NMD patients in a COVID-19 high-incidence area. Given the possibility of cyclical outbreaks of the infection, it will be important to offer alternatives to in-person care, redefine access to ancillary services and provide new approaches to support patients with chronic NMDs and their caregivers.

ACKNOWLEDGMENTS

The authors thank Associazione Amici del Centro Dino Ferrari for its support. This study was funded by Italian Ministry of Health, Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico Ricerca Corrente 2020 to NB and GPC. Open Access Funding provided by Universita degli Studi di Milano within the CRUI-CARE Agreement.

CONFLICT OF INTEREST

None of the authors has any conflict of interest to disclose.

AUTHOR CONTRIBUTIONS

Dr. D. Gagliardi had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Drs D. Gagliardi and G. Costamagna contributed equally and share the first authorship. Conception and design of the work: Delia Gagliardi. Acquisition, analysis and interpretation of data for the work: Delia Gagliardi, Gianluca Costamagna, Elena Abati, Eleonora Mauri, Roberta Brusa, Luigia Scudeller, Luca Andreoli, Gaia Citterio, Eleonora Piccin. Drafting of the manuscript: Gianluca Costamagna, Delia Gagliardi, Elena Abati. Critical revision of the manuscript for important intellectual content: Francesca Magri, Megi Meneri, Daniele Velardo, Stefania Corti, Giacomo Pietro Comi. Final approval of the version to be published: Monica Sciacco, Nereo Bresolin, Stefania Corti, Giacomo Pietro Comi.

ETHICAL PUBLICATION STATEMENT

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Delia Gagliardi https://orcid.org/0000-0001-8460-938X
Daniele Velardo https://orcid.org/0000-0003-1837-2788

REFERENCES

1. Beatriz Lara B, Carnes A, Dakterzada F, Benitez I, Piñol-Ripoll G. Neuropsychiatric symptoms and quality of life in Spanish Alzheimer's disease patients during COVID-19 lockdown. *Eur J Neurol*. 2020;27:1744-1747. https://doi.org/10.1111/ene.14339
2. Nguyen HC, Nguyen MH, Do BN, et al. People with suspected COVID-19 symptoms were more likely depressed and had lower health-related quality of life: the potential benefit of health literacy. *J Clin Med*. 2020;9(4):965. https://doi.org/10.3390/jcm9040965
3. Galea S, Merchant RM, Lurie N. The mental health consequences of COVID-19 and physical distancing: the need for prevention and early intervention. *JAMA Intern Med*. 2020;180(6):817-818. https://doi.org/10.1001/jamainternmed.2020.1562
4. Guidon AC, Amato AA. COVID-19 and neuromuscular disorders. *Neurology*. 2020;94(22):959-969. https://doi.org/10.1212/WNL.0000000000009566
5. Anand P, Slama MCC, Kaku M, et al. COVID-19 in patients with myasthenia gravis. *Muscle Nerve*. 2020;62:254-258. https://doi.org/10.1002/mus.26918
6. Costamagna G, Abati E, Bresolin N, Comi GP, Corti S. Management of patients with neuromuscular disorders at the time of the SARS-CoV-2 pandemic. *J Neurol*. 2020;268:1580-1591. https://doi.org/10.1007/s00415-020-10149-2
7. International MG/COVID-19 Working Group, Jacob S, Muppidi S, et al. Guidance for the management of myasthenia gravis (MG) and Lambert-Eaton myasthenic syndrome (LEMS) during the COVID-19 pandemic. *J Neurol Sci*. 2020;412:116803. https://doi.org/10.1016/j.jns.2020.116803
8. Solé G, Salort-Campana E, Pereon Y, et al. Guidance for the care of neuromuscular patients during the COVID-19 pandemic outbreak from the French rare health care for Neuromuscular Diseases Network. *Rev Neurol*. 2020;176(6):507-515. https://doi.org/10.1016/j.neurol.2020.04.004
9. Minotti C, Tirelli F, Barbieri E, Giaquinto C, Donà D. How is immunosuppressive status affecting children and adults in SARS-CoV-2 infection? A systematic review. *J Infect*. 2020;81:e61-e66. https://doi.org/10.1016/j.jinf.2020.04.026
10. Bersano A, Pantoni L. The impact of SARS-Cov-2 pandemic on stroke care: a warning message. *Eur J Neurol*. 2020;27:1781-1782. https://doi.org/10.1111/ene.14394
11. Mauri E, Abati E, Musumeci O, et al. Italian Association of Myology. Estimating the impact of COVID-19 pandemic on services provided by Italian neuromuscular centers: an Italian Association of Myology survey of the acute phase. *Acta Myol*. 2020;39(2):57-66. https://doi.org/10.36185/2532-1900-008.
12. Carrara C, Cappelletti L, Portalupi V. A view from the front line of the COVID-19 war. *Kidney Int*. 2020;98(1):10-11. https://doi.org/10.1016/j.kint.2020.04.018
13. Buttgereit F, Silva JAPD, Boers M, et al. Standardised nomenclature for glucocorticoid dosages and glucocorticoid treatment regimens: current questions and tentative answers in rheumatology. *Ann Rheum Dis*. 2002;61:718-722. https://doi.org/10.1136/ard.61.8.718
14. Zhang Y, Ma ZF. Impact of the COVID-19 pandemic on mental health and quality of life among local residents in Liaoning Province, China: a cross-sectional study. *Int J Environ Res Public Health*. 2020;17(7):2381. https://doi.org/10.3390/ijerph17072381
15. di Stefano V, Battaglia G, Giustino V, et al. Significant reduction of physical activity in patients with neuromuscular disease during COVID-19 pandemic: the long-term consequences of quarantine. *J Neurol*. 2020;268:20-26. https://doi.org/10.1007/s00415-020-10064-6
16. Strong MJ, Abrahams S, Goldstein LH, et al. Amyotrophic lateral sclerosis - frontotemporal spectrum disorder (ALS-FTSD): revised diagnostic criteria. *Amyotroph Lateral Scler Frontotemporal Degener*. 2017;18(3-4):153-174. https://doi.org/10.1080/21678421.2016.1267768

17. Consonni M, Telesca A, Dalla Bella E, Bersano E, Lauria G. Amyotrophic lateral sclerosis patients' and caregivers' distress and loneliness during COVID-19 lockdown. *J Neurol*. 2021;268:420-423. https://doi.org/10.1007/s00415-020-10080-6
18. Leung C. Risk factors for predicting mortality in elderly patients with COVID-19: a review of clinical data in China. *Mech Ageing Dev*. 2020;188:111255. https://doi.org/10.1016/j.mad.2020.111255
19. Delly F, Syed MJ, Lisak RP, Zutshi D. Myasthenic crisis in COVID-19. *J Neurol Sci*. 2020;414:116888. https://doi.org/10.1016/j.jns.2020.116888
20. Gao Y, Chen Y, Liu M, Shi S, Tian J. Impacts of immunosuppression and immunodeficiency on COVID-19: a systematic review and meta-analysis. *J Infect*. 2020;81:e93-e95. https://doi.org/10.1016/j.jinf.2020.05.017
21. Orcesi S, Ariaudo G, Mercuri E, et al. A new self-report quality of life questionnaire for children with neuromuscular disorders: presentation of the instrument, rationale for its development, and some preliminary results. *J Child Neurol*. 2014;29(2):167-181. https://doi.org/10.1177/0883073813511859
22. Burns TM, Graham CD, Rose MR, Simmons Z. Quality of life and measures of quality of life in patients with neuromuscular disorders. *Muscle Nerve*. 2012;46:9-25. https://doi.org/10.1002/mus.23245

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Gagliardi D, Costamagna G, Abati E, et al. Impact of COVID-19 on the quality of life of patients with neuromuscular disorders in the Lombardy area, Italy. *Muscle & Nerve*. 2021;64(4):474-482. https://doi.org/10.1002/mus.27378