



## Research Article

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# Changing Paradigm of Care of Neuromuscular Diseases in the COVID-19 Pandemic: A Scoping Review

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## Abstract

**Background:** In the current clinical scenario, people living with neuromuscular diseases (NMD) represent a vulnerable category with a high risk of severe course of COVID-19. Management of NMDs has become a challenge since most of them are chronic, disabling, progressive, and/or require immunosuppressive drugs. This scoping review aims to bring forth crucial queries for general neurologists and specialists dealing with NMD patients in the time of COVID-19 and highlight the research areas in a novel pandemic situation.

**Methods:** This scoping review was conducted according to the PRISMA- ScR statement. 18 research articles on neuromuscular disorders and effects of Covid-19 pandemic on rehabilitation and quality of life of these patients were included.

**Results:** Currently, clinical data regarding the effects of COVID-19 on people with NMDs and their risk of contracting the infection or experiencing severe manifestations of COVID-19 is scarce. There are notable differences in responses to disruptions across the world. The existing care delivery model from medical and on a continuum to rehabilitation is inherently different. The technological services in developing countries seem to be potentially compromised and unexplored to a great extent.

**Conclusion:** COVID-19 has already caused reorganization of neuromuscular clinical care delivery and education, likely having a lasting impact on the field. This paradigm shift has impacted all sectors of clinical, rehabilitation and research avenues of patients with NMD. Evolving healthcare delivery models in neurology during the pandemic are promising. After the initial phase of rapid adjustments, countries are now coming up with practical recommendations addressing the care of NMD patients during the pandemic. With this, patients with neuromuscular conditions can continue high level medical and rehabilitation care to remain healthy and thrive, during this pandemic.

**Keywords:** Neuromuscular diseases; Pandemic; COVID-19; Care, quality of life; Rehabilitation; Scoping review

**Abbreviations:** WHO: World Health Organisation; NMD: Neuromuscular Diseases; DMD: Duchenne Muscle Dystrophy; MG: Myasthenia Gravis; SMA: Spinal Muscle Atrophy; PA: Physical activity; QOL: Quality of Life

## Introduction

The WHO declared COVID-19 to be a “Public Health Emergency of International Concern (PHEIC)” on January 30, 2020, [1] and a pandemic on March 11, 2020 [2]. Covid-19 continues to act as a great burden for social and healthcare systems due to its unexpected contagiousness and severity of the clinical condition [3]. Overwhelming numbers of COVID infected patients have put a

significant strain on medical systems around the world, pushing the health-care system to its limit, forcing readjustment of standards of care for different pathologies.

Neuromuscular diseases (NMDs) are hereditary/acquired conditions affecting skeletal muscles, motor nerves, or neuromuscular junctions [4]. They are a heterogeneous group

of diseases in terms of aetiology, genetics, physiopathology, and treatments; and vary in severity and disease progression [5,6]. Most NMDs show prevalence rates between 1 and 10 per 100,000 population, except for some rare types [7]; and account for 2.8-18% of referrals in the neurology department [8]. Hereditary forms of NMD manifest at birth or early childhood whereas the incidence of other forms increases with age [9]. On an international level, an aging population means the prevalence of NMD is likely to increase. These disorders result in longstanding functional deficits that result in substantial utilization of healthcare resources in addition to the emotional, financial and social burden to those affected individuals and their families. In the current COVID scenario, people living with neuromuscular diseases are identified as a vulnerable category and are having several implications on NMD progression, with and without SARS-CoV-2 infection. Their management is challenged because many of them are complex, chronic, disabling diseases, follow a progressive course and require immunosuppressive drugs. Neurological care is a spiral management process and is effective when initiated at an early stage; constantly revised and updated with an appropriate and timely follow-up. Long-term approach ensuring continuity of care is integral to highest possible recovery and maintenance of function. This ideal approach already remains an unmet need and COVID-19 pandemic has further magnified the pre-existing challenges. Intensifying the inequalities, the coronavirus 2019 (COVID-19) pandemic has potential to disproportionately and severely affect patients with neuromuscular disorders. Overall, this pandemic has resulted in a significant disruption of clinical and support services for patients with NMDs, affecting their already disturbed quality of life. As the third wave of the pandemic progresses, clinicians and researchers should address these crucial open issues to ensure adequate caring for NMD patients and to ensure optimal quality of life for them. This scoping review aims to summarize the available evidence so far and bring forth crucial queries for general neurologists and specialists dealing with NMD patients in the time of COVID-19; address routine and emergency medical and rehabilitation services, and other considerations for the patients with neuromuscular conditions during the COVID-19 pandemic; and highlight the research areas in a novel pandemic situation.

## Methodology

This scoping review was conducted according to the PRISMA-ScR [10] statement where applicable.

It involved steps outlined below:

1. formulating a research question;
2. establishing inclusion criteria to identify and include studies;
3. identification of relevant studies across the available range of potential evidence;
4. independent and objective screening and selection of studies for inclusion;

5. extraction and charting of the data according to key concepts identified; and
6. summarization of the findings for clinical relevance and future research.

## Inclusion Criteria

To be included in the review, studies met the following criteria:

- Publication type: papers published in online peer reviewed journals; full length
- Studies on Neuromuscular disorders and effects of Covid-19 pandemic on rehabilitation and quality of life of these patients were included.
- Language: the studies written in English.
- Duration till May 2021.

## Information Sources

Studies were identified by searching the following electronic databases: Google Scholar, Cochrane, Pubmed, EBSCO, and CINAHL. The search was conducted over a period of two months. In addition, reference lists of the included studies were screened for potentially eligible studies.

### Search Strategy:

The search strategy was to include the study population using terms and keywords prior decided: The following MESH terms were used for the search:

[Neuromuscular diseases], [Paediatric/Adult], [Covid-19/pandemic], [NMD], [Rehabilitation in NMD], [Quality of life in NMD]

### Study Selection:

Study selection was initially performed by the first author and then checked by the second author. First, the titles and abstracts of the publications retrieved by electronic searching were screened. Second, potentially eligible studies were retrieved full text before definitive inclusion.

### Data Extraction:

Data was extracted from the studies by the first author and then checked by the second author. The extracted data was discussed until consensus was reached. No specific form was used for data extraction; however, the outcomes to be extracted were defined prior.

The following information was extracted from each study:

- a) Author and year of publication,
- b) Study design,
- c) NMD studied
- d) Area addressed

### Analysis:

The results were presented using a 'narrative review' of the

process-oriented data and simple quantitative analysis using descriptive statistics.

### Risk of bias in individual studies:

Risk of bias for each included trial was independently assessed by the same initial reviewers. The findings were discussed between the two authors in situations of disagreement, until a consensus was reached.

## Results

The initial search revealed 75 articles in all, out of which 22 were duplicates. The articles were then screened by two reviewers; 16 articles were excluded. The article titles, abstracts and full text of the 37 remaining articles were then reviewed. Of the 37, 21 articles were relevant to our area of study. 18 of those articles could be retrieved as full texts and met the inclusion criteria. These were included in our final review. The primary reasons for excluding articles were that they were duplicate articles, full text of the articles could not be retrieved and they did not meet the inclusion criteria.

Out of the 18 articles selected, 4 were retrospective studies, 14 were review studies. Given the inadequacy of scientific literature on NMD in the recent pandemic situation, information published on social media such as news, reports, blogs, letters, etc. (in the past two months April and May 2021) is also included to support the views of the authors.

## Discussion

This review process provides an overview of the following key areas:

1. Existing literature on NMD in COVID-19
2. Supporting evidence prior to COVID-19
3. Directions for future research

### Risk of infection causing a new NMD

There is a known risk attributable to certain viral infections (e.g., influenza, H1N1, Zika, Epstein-Barr virus) with a rationale that molecular mimicry exists between specific viral proteins and proteins on peripheral nerves (e.g., gangliosides) leading to an innocent bystander attack against the myelin or axon of peripheral nerves; however, direct causality is uncertain. There is no current evidence of direct viral invasion with inflammation and degeneration of motor neurons and peripheral nerves as seen in some viral infections (e.g., poliovirus, enterovirus D68, West Nile, herpes zoster, cytomegalovirus). Nevertheless, it is possible that the virus may be neurotropic and directly infect and damage motor neurons and peripheral nerves. [11,12].

### COVID-19 and NMD

**Risk of COVID-19 in NMD:** In this clinical scenario, people living with NMD represent a vulnerable category with a high risk of a severe course of COVID-19. These documents define the risk of a severe course of Covid-19 as high or moderately high in all NMD

patients, apart from those with the mildest forms. Specific factors conferring a high or very high risk of developing severe COVID-19 complications include respiratory insufficiency, cardiac disease, obesity, and immunocompromised status due to chronic steroid treatments in certain patient populations with neuromuscular conditions [13]. Some more factors identified are extrapolated from the general population based on other demographic factors or health considerations. Queries related to continuation of immunosuppressive and immunomodulatory therapies yet remain unanswered. Some clinicians have pointed towards the protective role of these therapies. Patients with NMDs such as Duchenne Muscular Dystrophy (DMD) and Spinal Muscular Atrophy (SMA), are more medically fragile and have higher health care needs than the adult population. It is worth pointing out that highly-dependent patients needing help from caregivers in basic activities of daily living such as dependence in hygiene, mobilization and feeding, present an increased risk due to their impossibility to isolate. In general, the paediatric population has shown to be less severely impacted with lower infection rates and lower morbidity and mortality rates than the adult population, however, as expected, children with underlying medical conditions are at higher risk of morbidity from COVID-19 than their peers [14]. Risk assessment and stratification are crucial to identify NMD patients who are at increased risk to suffer from severe COVID-19 complications [15]. Currently, clinical data regarding the effects of COVID-19 on people with NMDs and their risk of contracting the infection or experiencing severe manifestations of COVID-19 is scarce. We recognize that this theoretical concern is expressed in editorial or communications to journals and remains unsupported by peer reviewed published literature of COVID-19.

**COVID-19 vaccine efficacy and risk in NMD:** Currently, no data is available on vaccination of disease-specific neuromuscular groups. Such data during this time on risk for and outcomes of COVID-19 in these groups will greatly inform risk stratifications in the future and will guide vaccination programmes for NMD patients. Whether immunosuppressive or immunomodulatory therapy will make the COVID-19 vaccines less effective is highly relevant for patients with NMDs and will need study. Pragmatically, we will also need to consider how patients with NMD receiving telemedicine or who are self-isolating will receive vaccination, when available.

**Certain national and international neurologic and neuromuscular networks:** have produced consensus recommendations and guidance to help both NMD patients and families and their physicians to prevent and manage SARS-CoV-2 infection in this category. NMD displays varying levels of disability in people with the same diagnosis, thus it is difficult to give COVID-19 related general recommendations. Specific guidelines have been developed for the management of myasthenia gravis (MG) and Lambert Eaton myasthenic syndrome (LEMS) [16], DMD and SMA [17,18]. They highlight the importance of collaborative treatment decisions between the patient, family, and health-care provider, considering any geographic or institution-specific policies

and precautions for COVID-19.

### COVID-19 physical activity (PA) & Quality of life (QOL)

NMD patients need to perform regular PA to counteract the negative consequences of the disease to maintain optimal levels of functioning and QOL. The impact of COVID-19 on physical activity (PA) & QOL in NMD patients need to be addressed. Quarantine restriction has caused a sudden change in people's lifestyle, leading to increased sedentary behaviour and decreased physical activity (PA) in these patients. Moreover, a significant difference in the total weekly PA level was found depending on the presence of NMD, impaired walking, gender and BMI. Also, a correlation between SF-12 scores and the entity of the reduction of PA level, confirmed a relevant association with the quality of life in NMD. Research also suggests a relevant association with the quality of life in NMD [15]. A recent review paper highlights that COVID-19 is a physiological challenge with significant health risks [19]. It discusses the impact of sedentarism due to the COVID-19 home confinement on neuromuscular, cardiovascular and metabolic health supporting evidence of inactivity with physiological and pathophysiological implications. Just a few days of sedentary lifestyle are sufficient to induce muscle loss, neuromuscular junction damage and fibre denervation, insulin resistance, decreased aerobic capacity, fat deposition and low-grade systemic inflammation. Notably, muscle atrophy is a very fast phenomenon detectable after just two days of inactivity. There is now increasing evidence that chronic inactivity, caused by bed rest for example, triggers neurodegenerative processes inducing muscle fiber denervation and damage to the neuromuscular junction and also that innervation and muscle-nerve cross-talk, are compromised. For the NMD population, COVID-19 represents a precipitating factor of muscle wasting, atrophy, and tightness through the limited PA. The major concern for clinicians and researchers alike is if COVID has induced clinical worsening. For example, has this situation affected the ambulatory potential of a patient with DMD?

Considering the recency of this situation, long term consequences on the disease progression remain largely unknown and need to be monitored qualitatively and quantitatively. Nonetheless, the evidence that exercise is of vital importance for preserving the integrity and function of the neuromuscular system is incontrovertible. This supportive evidence emphasizes the need for physical activity as a countermeasure programme to preserve as much as neuromuscular health and other physiological functions in NMD patients.

### Disruption of essential neuro care services

Disruption of essential neuro rehabilitation interventions/services have been reported in many countries. Although no country reported full closure of all neurorehabilitation services, disruptions of essential, emergency and life-saving NMD services were reported by a majority of them. Some preliminary surveys assessed changes in the provision of pharmacological therapies,

outpatient clinical and instrumental services, support services (physiotherapy, nursing care, psychological support) and clinical trials [20]. Majority of the neuromuscular centres reported a reduction in outpatient visits and examinations, postponed in-hospital administration of therapies, and suspended diagnostic and support services. Rehabilitative services were found to be most affected as on-site outpatient visits were suspended in the majority of the centres. Community-based outpatient services, prevention and promotion of maintenance health services, and services for specific age groups such as older adults and children, were among the most severely disrupted [13,18].

### Disability inclusive response to COVID-19

People with NMD have unmet health needs; resource and access barriers which have magnified due to COVID-19 circumstances [8]. There is a need to actively reach out to the people with NMD as a 'disability inclusive response to COVID-19'. Neurorehabilitation is recognized by majority countries as an integral component of their national COVID-19 response plans. Two-thirds of countries have a multisectoral neurorehabilitation co-ordination platform for COVID-19 response, however, most countries are lacking additional funding for these plans [21]. The clinical spectrum of neuromuscular disorders as well as the existing care delivery model from medical and on a continuum to rehabilitation is inherently different between the countries. Notable differences in responses to disruptions were observed across the world.

### Learned lessons are emerging

In parallel, the reorganization of hospital and outpatient services has changed the management of non-infected NMD patients and their caregivers, favouring at-distance approaches. The world is responding to the disruption of neurorehabilitation services in innovative ways, such as telemedicine, teletherapy interventions, and hotlines with training for health care providers. Strategies adopted by neuromuscular centres to overcome these changes included maintaining urgent on-site visits, addressing patients to available services and promoting remote contact and telemedicine [20,22]. Though telemedicine services have vastly grown over the past year, there is still better scope for its promotion and improvement. A close collaboration between the different neuromuscular centres and service providers as well as further implementation of telehealth platforms are necessary to ensure quality care to NMD patients in the near future and in case of recurrent pandemic waves [17]. However, the literature on the validation of telehealth in this subgroup of patients is scant. Telemedicine and telerehabilitation demonstrate a promising alternative strategy, but this seems to be potentially compromised and unexplored to a great extent in developing countries. Many patients with neuromuscular disease rely heavily on caregiver support throughout their lifetime and thus maintaining the health of their primary caregivers is also a significant consideration in the health and well-being of the patients [23,24].

## Need for ethical decision making

There is an increased need for ethical decision making in the absence of set guidelines. It is important for key decision-makers and policymakers to be aware of the current developments for children and adults with rare diseases such as inherited neuromuscular disorders so that individual patient decisions and policies are grounded by accurate clinical information [23]. In recent years, the long-term prognosis of children and young adults diagnosed with chronic neuromuscular disorders has changed dramatically from comfort care to therapeutic and supportive interventions [25]. Supportive care has become increasingly sophisticated and multidisciplinary with aggressive monitoring and treatment for the manifold complications of these diseases. Options for respiratory support have expanded and significantly improved the quality of life and life expectancy. This underlines the need for resource allocation decisions and restraints on neurological care; and caution in developing institutional or public health policies on ethical grounds [23,26].

## Recommendations for rehabilitation

Rehabilitative therapy services including physical, speech, and occupational therapies were halted due to the pandemic. Some of these services as well as psychological and behavioural care can be delivered via telehealth when appropriate. Patients, physicians, and therapists need to jointly discuss the urgency of these therapies and their suspension or continuation on a case-by-case basis. Additionally, home therapies and exercise, such as intermittent bracing, therapeutic positioning, and increased physical activity in the home and neighbourhood should be considered. It should be noted that during the pandemic, the “parent/caregiver has been forced to assume the sole responsibility of all the in-person therapy services that were previously provided by the therapists” [27]. Combined with the range of other stressors associated with the current pandemic and ongoing care of individuals with NMD, these added responsibilities may be exhausting and difficult for caregivers to manage. Providers involved in the ongoing care of patients with NMD should take this into consideration when making treatment recommendations [26,27].

## Impact on research

The natural history of certain childhood neuromuscular disorders is not necessarily predictable by their initial presentations, and more frequent monitoring and follow-up is required to decide the line of management. Also, lack of homogeneity and delay in diagnosis and all the factors as mentioned above affect the research avenues of already fragile research in NMD [25]. The pandemic has forced a shift in their methodologies and data collection strategies. The above changes to an approved protocol are considered as protocol deviations (albeit minor given the situation). Thus, the already fragile medical research in this population is further impacted affecting the ongoing trials as well as curtailing new research avenues. Currently, multiple clinical

trials are in progress for NMDs and it is recommended that any decision regarding ongoing need for in-person evaluations and treatments be based with consideration for patients' best interest [16]. The clinical researcher weighs risks and benefits with each individual participant in each clinical trial. Collaborative efforts among institutions will help generate the data needed to inform management of rare NMDs in the setting of COVID-19 and maintain clinical trials and research despite current challenges. Primary goals of clinical research during this time are to develop evidence-based best practices and to minimize morbidity and mortality related to COVID-19 for patients with neuromuscular disorders. More research focussing on the NMD patients without SARS-CoV-2 infection is equally needed. Many of the responding countries are not collecting any data on neuromuscular disorders or its manifestations in people with COVID-19, and fewer than one-tenth of countries are researching COVID-19 effects on their health. The paucity of literature in the NMD population during the pandemic era in developing countries also needs to be addressed.

## Conclusion

The review has suggested that COVID-19 has caused massive reorganization of neuromuscular clinical care delivery and education, for both with and without SARS-CoV-2 in these patients. COVID-19 paradigm shift has impacted all sectors of clinical, rehabilitation and research avenues of patients with neuromuscular diseases having a lasting impact on the field. However, on a positive note, evolving healthcare delivery models in neurology during the pandemic are promising. After the initial phase of rapid adjustments, countries are now coming up with practical recommendations addressing the care of NMD patients during the pandemic. Concern regarding the effects of COVID-19 on people with neuromuscular conditions is largely theoretical and remains unsupported with clinical data. Limited preliminary observations cannot support a definitive conclusion as to whether patients with NMD should be considered a high or low-risk group for COVID-19, however, they encourage an optimistic view. Risk assessment and stratification are crucial for ethical decision making in the absence of set guidelines. Risk/benefit analysis should be done on a case by case basis and in the best interest of the individual with NMD. Though strong evidence is lacking, it is recommended that NMD patients already on immunosuppressive medications practice extra-vigilant social distancing, avoiding public gatherings/crowds and crowded public transport, and use alternatives to face-to-face consultations (e.g., telemedicine), if clinically appropriate. Continuity of care for this population needs to be ensured with “careful adherence to public health recommendations, careful management of acute medical issues, and use of telehealth technology” to maintain optimal health during this pandemic. Through this review, we highlight the importance of collaborative treatment decisions between the patient, family, and health-care providers, considering any geographic or institution-specific policies and precautions for COVID-19. We advocate for continuing multidisciplinary care for these patients using telehealth. With

these, patients with neuromuscular conditions can continue high level medical and rehabilitation care to remain healthy and thrive," during this pandemic.

Limitations and Future research: Living with NMD is a challenge not only for patients but for their caregivers and families, and COVID-19 pandemic situation represents even a greater stress test. There is a dearth of data on the reaction of NMD patients to COVID-19. The literature identified reflects clinicians and policy makers' views, however this should be complemented by patients' & caregivers' perspectives. The collateral damage of COVID related home confinement and social distancing measures on the mental health of patients and their caregivers needs to be equally addressed. One of the many faces of the catastrophic COVID-19 situation is its social, occupational and economic impact in NMD patients and their families. Considering geographic & cultural variations in the bio-psycho-social-structure, context-specific epidemiological studies should be conducted and need to be documented country region wise. In particular, rehabilitation interventions for patients with NMD after COVID-19 are lacking. Proposed utility and appropriateness of telemedicine should be explored, especially in developing countries. To monitor at distance approaches, patient/caregiver reported outcome tools need to be developed. The lag in medical access and rehabilitation services and facilities and its impact on the progression of the disease needs to be identified qualitatively and quantitatively. The question needing critical attention is how the lag in medical access and rehabilitation services and facilities have impacted the progression of the disease itself. e.g. has this impacted the ambulatory potential of a patient with DMD? Similar concerns raise clinical questions for future investigation. This scoping review highlighted the vivid aspects of the situation in the context of neuromuscular conditions & COVID-19. Future threads to this discussion will be interesting to follow.

### Conflict of Interest

No conflict of interest noted by the authors.

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