

# Impact of SARS-CoV-2 Infection Among Non-Invasive Ventilated ALS Patients

Miguel Oliveira Santos<sup>a,b,\*</sup>, Sara Domingues<sup>c</sup>, Marta Gromicho<sup>b</sup>, Susana Pinto<sup>b</sup> and Mamede de Carvalho<sup>a,b</sup>

<sup>a</sup>*Institute of Physiology, Instituto de Medicina Molecular, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal*

<sup>b</sup>*Department of Neurosciences and Mental Health, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisbon, Portugal*

<sup>c</sup>*Department of Physical Medicine and Rehabilitation, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisbon, Portugal*

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## Abstract.

**Background:** The impact of SARS-CoV-2 infection among neuromuscular diseases with respiratory involvement, including amyotrophic lateral sclerosis (ALS), is still to be elucidated.

**Objectives:** We aim to characterize the clinical outcome of ALS patients non-invasive ventilated (NIV), following SARS-CoV-2 infection.

**Methods:** We analyzed retrospectively our patients followed regularly at our ALS clinic, from the beginning of the COVID-19 pandemic (middle March 2020) to March 2021. We included patients on NIV with a documented SARS-CoV-2 infection. We recorded demographic and clinical data, including from the acute infectious illness.

**Results:** Three men with spinal-onset ALS are described, mean age of onset was  $55 \pm 9.1$  years (45–61), and mean disease duration was  $17.5 \pm 15.9$  months (6.1–41). All of them were wheelchair-bounded, with a mean ALSFRS-R of  $15.3 \pm 0.6$  (15–16). One patient used NIV 15 hours/day, 2 between 4 to 7 hours/day, and all used assisted coughing twice daily. None had coexistent comorbidities. They were managed for SARS-CoV-2 infection as outpatients with fluticasone, bronchodilators, azithromycin and increasing frequency of assisted coughing. Supplemental oxygen (mean of 2 liters per minute) was needed in two patients, and one required NIV also during the daytime. Total recovery from SARS-CoV-2 infection was observed in all, despite being in an advanced stage of their disease, with severe respiratory involvement.

**Conclusions:** Prompt medical treatment is recommended for ALS patients with severe disease infected by SARS-CoV-2.

**Keywords:** Amyotrophic lateral sclerosis, SARS-CoV-2, COVID-19, non-invasive ventilation, respiratory complications

## INTRODUCTION

The novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first

identified in December 2019 in the city of Wuhan (China) [1]. SARS-CoV-2 infection has caused an outbreak of the underlying disease, Coronavirus-Disease-19 (COVID-19), which has continued to spread rapidly throughout China and then worldwide. The most common symptoms of COVID-19 are fever, cough, and fatigue; however, in more severe cases, patients may develop pneumonia, acute respiratory distress syndrome and even multiorgan failure, eventually leading to death [2].

\*Correspondence to: Miguel Oliveira Santos, Department of Neurosciences and Mental Health, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisbon, Portugal. Avenida Professor Egas Moniz, 1649-028 Lisboa, Portugal. Tel.: +351 964919683; E-mail: migueloliveirasantos@hotmail.com.

It has been reported that concomitant chronic diseases are strongly associated with COVID-19 severity, in particular arterial hypertension, diabetes, cardiovascular, respiratory and chronic kidney disease [3, 4]. In addition, obesity has also been found as a predictor for poor prognosis [5, 6]. However, little is known about the impact of SARS-CoV-2 infection among neuromuscular diseases, including amyotrophic lateral sclerosis (ALS). We aim to characterize the clinical outcome of ALS patients with severe respiratory compromise following SARS-CoV-2 infection.

## METHODS

We analyzed retrospectively ALS patients followed regularly at our ALS clinic, from the beginning of the COVID-19 pandemic (middle March 2020) to 31st March 2021. We included patients with ALS, as defined by the new Gold Coast criteria [7]. We included patients on non-invasive ventilation (NIV, overnight or longer) with a positive nasopharyngeal exudate for SARS-CoV-2 determined by reverse-transcription polymerase chain reaction. We recorded clinical data, including gender, onset age, onset region, disease duration, functional status (ALSFRRS-R), number of hours on NIV and comorbidities. COVID-19 symptoms, management and support treatment were also recorded.

All procedures were performed in accordance with ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

## RESULTS

Three sporadic ALS patients (1.5%) were included from a total of 204. All of them were men with spinal-onset, the mean age of onset was  $55 \pm 9.1$  years (range, 45–61) and the mean disease duration

was  $17.5 \pm 15.9$  months (range, 6.1–41). The mean ALSFRS-R score was  $15.3 \pm 0.6$  (range, 15–16) and all of them were wheelchair-bounded. Patient 2 was dependent on NIV for at least 15 hours daily and patient 3 did not tolerate well nocturnal NIV (maximum usage of 4 hours) – Table 1. All used assisted coughing with a mean of twice daily. None had particular comorbidities, including arterial hypertension, diabetes, cardiovascular, lung or chronic kidney disease. One patient was living in skilled nursing facilities, while the remaining were in their own homes.

SARS-CoV-2 transmission occurred through facility outbreak or a familial positive contact. Fever, cough, and increase respiratory fatigue with percutaneous oxygen desaturation (89–92%) were the main COVID-19 symptoms. Only one patient stayed in the urgency yard for two days following SARS-CoV-2 infection, but all of them were managed as outpatients. Supplemental oxygen was needed in two patients (2 liters per minute). An additional one required NIV also during the daytime. It is noteworthy to mention that patient 3 needed ventilation parameters adjustment, in particular increased expiratory positive airway pressure, which have compromised even more its compliance to NIV during the acute phase. Increased frequency of assisted cough device usage was required. Two inhaled fluticasone 250 µg 2id was added to the previous used bronchodilators (salbutamol and ipratropium) plus prophylactic azithromycin *per os* 500 mg daily for up to three days. Nocturnal oximetry and NIV usage before, during and 30 days after SARS-CoV2 infection and treatment support through the acute phase are summarized in Tables 1 and 2, respectively.

This study has some limitations, in particular the low number of infected ALS patients. In addition, there is no information regarding pulmonary imaging data during the acute phase of SARS-CoV2-2 infection, because thoracic scans were not performed. On the other hand, as the ALS patients were managed as outpatients, we have not enough data to calculate

Table 1  
Nocturnal oximetry results and non-invasive ventilation usage before, during and 30 days after SARS-CoV2 infection

	Baseline		Acute phase		30 days after	
	Nocturnal oximetry	NIV usage*	Nocturnal oximetry	NIV usage	Nocturnal oximetry	NIV usage
Patient 1	94%	7 h	89%	14 h	94%	14 h
Patient 2	93%	15 h	89%	20 h	92%	16 h
Patient 3	93%	4 h	92%	2 h	93%	7 h

\*Non-invasive ventilation average usage.

Table 2  
Treatment management during SARS-CoV2 infection

	Mucolytics	Bronchodilators + Fluticasone*	Cough- assist* <sup>2</sup>	Prophylactic azithromycin* <sup>3</sup>	Ventilation parameters adjustment	Oxygen support
Patient 1	X	X	X	X	–	2 L/min for up 20 days
Patient 2	–	X	X	X	–	2 L/min up to 15 days
Patient 3	–	X	X	X	X	–

\*<sup>3</sup>Bronchodilators (four inhaled salbutamol plus ipratropium)+two inhaled fluticasone 250 µg 2id; \*<sup>2</sup>Increase usage; \*<sup>3</sup>500 mg/daily for up three days.

SARS-CoV-2 severity score. In Portugal, infected outpatients are not routinely submitted to SARS-CoV-2 test to declare cure, so we do not know the actual number of days of positivity.

All patients recovered from the SARS-CoV-2 infection without additional complications, returning to their baseline condition, after a mean time of one month. In fact, patient 1 could have reduced NIV usage following SARS-Cov2 infection if he would accept changing a nasal to a facial mask. On the other hand, patient 3 have its NIV parameters adjustment to the baseline level, and now have a better compliance.

## DISCUSSION

Reviewing the literature few reports of patients with neuromuscular disorders and affected by COVID-19 have been published. The outcome of patients with myasthenia gravis was positive [8]. It is reasonable to anticipate that patients with poor respiratory function have an increased risk of severe complications when infected by SARS-CoV-2. However, one recent study concluded that patients with chronic obstructive pulmonary disease and emphysema hospitalized with COVID-19 may not have worse outcomes [9].

To our best knowledge, this is the first report describing the clinical outcome ALS patients with severe respiratory impairment, and with symptoms related to SARS-CoV-2 infection. In this small cohort, it is noteworthy that all patients have survived COVID-19 despite being in an advanced stage of the disease, depended on NIV. On the other hand, comorbidities commonly associated with COVID-19 severity were absent in our patients. Our findings support that prompt medical care is recommended in patients with severe ALS disease and SARS-CoV-2 infection and indicates that the outcome can be favorable in spite of the severe respiratory insufficiency.

## DECLARATION OF INTEREST

None of the authors have potential conflicts of interest to be disclose.

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