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Parkinsonism and Related Disorders 86 (2021) 78–80

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Correspondence

Effects of COVID -19 pandemic and lockdown on people with multiple system atrophy participating in a therapeutic education program

ARTICLE INFO

Keywords
MSA
COVID-19
Lockdown
Semi-structured questionnaire
Motor and non-motor symptoms
Admission
Fatality

COVID-19 has been widely studied in people with Parkinson's disease (PwPD) [1], but besides a study including only nine people with multiple system atrophy (PwMSA) in a cohort of mostly vascular parkinsonism cases [2], information is lacking on COVID-19 outcomes in PwMSA.

In this descriptive multiple-centre study, we included 32 participants in a therapeutic education program during December 2019–February 2020, consisting of 16 PwMSA fulfilling the diagnostic criteria of probable MSA and their respective 16 main caregivers. We classified PwMSA with the disability UMSARS sub-scale as early-intermediate vs. advanced. In July 2020, after the first pandemic wave, we reviewed the clinical charts and administered a semi-structured phone-questionnaire focusing on infection, hospital-admission, symptoms worsening, and perceived impact of the lockdown (Suppl-Table 1). The ethics committee approved the study. All participants signed the informed consent. Data are expressed as absolute and relative frequencies or median and interquartile range (IQR) and compared by Fisher's or Mann-Whitney's *U* test as appropriate. Statistical significance was $p \leq 0.05$.

Baseline features in PwMSA were: women = nine (56%); median age-at-onset = 55 (IQR = 48–59); median age-at-inclusion = 60 (IQR = 56–66); median disease-duration = 5 (IQR = 4–7) years; median UMSARS-2 = 24 (IQR = 20–38). Eight (50%) had parkinsonian MSA variant (MSA-P). Eight were in early-intermediate stage (50%). Eleven (68.7%) were following physical and/or speech therapy sessions weekly. Baseline features among caregivers were: women = seven (44%), median age-at-inclusion = 57 (IQR = 40–59) years (no significant differences with PwMSA).

Fig. 1-A shows the study flow-chart and Suppl Fig 1-A-D data of infection, admissions and fatality in PwMSA. Frequency of symptomatic COVID-19 was 6% (a respiratory infection case requiring admission, with good recovery). The other three participants who underwent PCR due to respiratory symptoms were negative (75%). Five (31%) were admitted: two due to respiratory infection, two urinary infection and one sudden respiratory failure. Median admission duration was 9 days (IQR = 2–23). Admitted cases had significantly higher UMSARS-2 scores (median = 38.00; IQR = 29.50–43.00) than the rest (median = 22.5; IQR = 17.25–25.25, p = 0.013). Fatality was 25% (N = 4). No autopsies were performed. Three died during the first wave. The cause of death was sepsis (N = 1), sudden death (N = 2, one of whom had been just diagnosed with locally disseminated endometrial cancer after a respiratory infection with negative SARS-CoV-2 PCR), and hyperacute respiratory syndrome (N = 1, a patient who died within 24 hours of admission at a stage when PCR for SARS-COV-2 was not widely applied yet in our country, not allowing to rule out COVID-19). One was early-intermediate (12.5%), and three were advanced (37.5%; p = 0.57). Two had MSA-P (50%). Median age-at-onset, age-at-inclusion, disease duration and UMSARS-2 did not differ between participants who died and survivors (data not shown). No caregivers had symptoms, tested positive, were admitted, nor died.

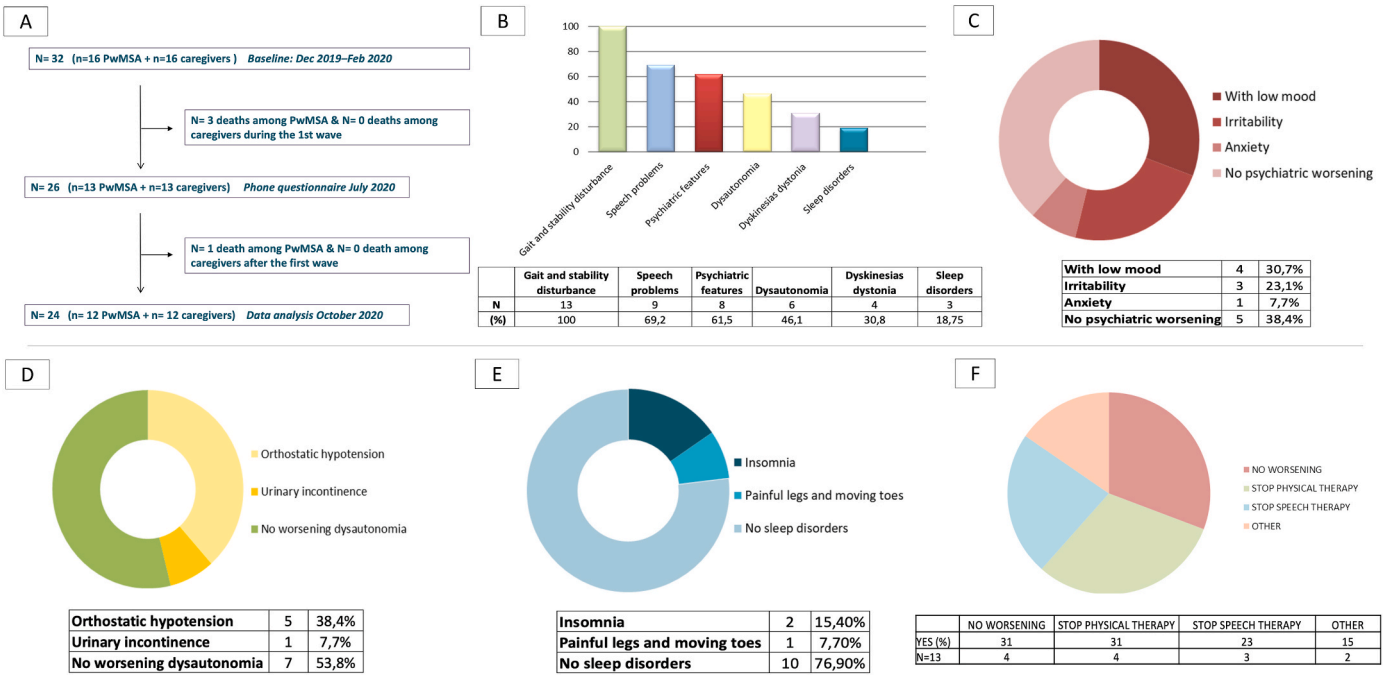
Among the 13 PwMSA surviving the first wave, symptoms that worsened most were gait (100%), speech (69.2%), psychiatric (61.5%), dysautonomic (46.1%), dyskinesia (30.7%), and sleep (23%) features (Fig. 1-B,C,D,E). Among caregivers, 46% reported anxiety.

Of these 13 PwMSA, 31% considered that they worsened due to stopping physiotherapy, 23% due to interruption of speech therapy and 15% due to other (social and family) problems (Fig. 1-F).

To the best of our knowledge, besides a prior survey of different parkinsonisms [2], this is the first specific study of PwMSA during the COVID-19 pandemic. The frequency of COVID-19 was 6%, similar to PwPD [1]. This low figure could be due to important motor disability and strict lockdown, as suggested for advanced PD [1]. Fatality in about six months was 25%, higher than the ~10% of the six-month follow-up periods in the European and American MSA natural history studies, and median disease-duration of deceased participants was 6.5 years in contrast to 9.8 years in the aforementioned studies [3,4]. These differences might be related to the pandemic and lockdown setting, or, alternatively, could be merely stochastic in the setting of small sample.

Frequent worsening of gait, speech and dysautonomia are in line with MSA natural history. Additionally, low mood, irritability, anxiety and insomnia are not surprising in the pandemic and lockdown context.

https://doi.org/10.1016/j.parkreldis.2021.03.021
Received 30 December 2020; Received in revised form 12 March 2021; Accepted 20 March 2021
Available online 29 March 2021



	Gait and stability disturbance	Speech problems	Psychiatric features	Dysautonomia	Dyskinesias dystonia	Sleep disorders
N	13	9	8	6	4	3
(%)	100	69,2	61,5	46,1	30,8	18,75

With low mood	4	30,7%
Irritability	3	23,1%
Anxiety	1	7,7%
No psychiatric worsening	5	38,4%

Orthostatic hypotension	5	38,4%
Urinary incontinence	1	7,7%
No worsening dysautonomia	7	53,8%

Insomnia	2	15,40%
Painful legs and moving toes	1	7,70%
No sleep disorders	10	76,90%

	NO WORSENING	STOP PHYSICAL THERAPY	STOP SPEECH THERAPY	OTHER
YES (%)	31	31	23	15
N=13	4	4	3	2

Fig. 1. Panel A: Flow-chart showing the participants survival outcome. Panel B: Bar diagram showing the percentage of participants with different categories of motor and non-motor symptoms worsening. Panels C, D and E: Ring diagrams showing the percentage of the specific psychiatric (C), dysautonomic (D), and sleep (E) worsening. Panel F: Pie diagram showing the reasons for worsening during the lockdown as perceived by PwMSA.

Anxiety was also frequent among caregivers, probably due to the burden of caregiving and social isolation. The fact that more than 50% of PwMSA perceived that the lockdown was harmful due to interruption of physiotherapy and speech therapy is in line with a recently published study where physiotherapy was helpful in MSA [5].

The main limitation of this study is the small sample inevitable in a rare disease such as MSA. Also, only PwMSA with respiratory symptoms were PCR-tested for SARS-CoV-2, since at the time of the first pandemic wave in our country PCR was only applied to people with symptoms; hence we cannot rule out additional cases of asymptomatic COVID-19 in our cohort. This limitation is important when interpreting fatality, as only one of the four deceased cases had a negative PCR for SARS-CoV-2. Due to the lockdown restrictions, no autopsies were performed and we used an "ad-hoc" short semi-structured questionnaire instead of published and validated questionnaires. As strengths this is the first study specifically describing MSA outcomes during the pandemic and lockdown, and the semi-structured questionnaire asked open questions to avoid inducing replies.

In conclusion, we recorded a single case of COVID-19 infection, yet the mortality was 25%. Gait, speech and psychiatric features were the symptoms that worsened most. Impairment during the lockdown was related to interruption of physical and speech therapies according to the perception of PwMSA.

Data availability

Data can be shared with a qualified researcher upon reasonable request, following an approval by the responsible ethical committee.

Declaration of competing interest

The authors have no conflicts of interest relevant to this particular study.

Acknowledgements

We are most grateful to all the participants, as without their generosity none of this research would have been possible. This study is part of a project funded by the PERIS (Pla Estratègic de Recerca i Innovació per la Salut) 2019–2020 from Departament de Salut de la Generalitat de Catalunya (PI: A Cámara; SLT008/18/00191). The co-authors from Parkinson's Diseagse & Movement Disorders Unit, Hospital Clinic are members of the European Reference Network for Rare Neurological Diseases – Project ID No 739510. Our institution is supported by the CERCA programme of the Generalitat de Catalunya.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.parkreldis.2021.03.021.

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