COVID-19 impact on consecutive neurological patients admitted to the emergency department

INTRODUCTION

The outbreak of SARS-CoV-2 hit Italy by the end of February and rapidly spread from Lombardy to the rest of the country, with a number of fatalities beyond 31 000. Although all regions have reported having patients with COVID-19, the highest number of identified cases was in the provinces of eastern Lombardy.[1] Several case reports and small series also suggested an association between COVID-19 and cerebrovascular events, and immune or inflammatory-mediated peripheral and central nervous system (CNS) involvement.[2 3]

To date, however, no comprehensive large surveys on the impact of COVID-19 on neurological status of patients presenting at the emergency room have been published. In fact, still little is known on which are the most common acute neurological presentations in COVID-19 and whether they differ compared with patients without COVID-19 in terms of severity and outcomes.

The urgent drift to cope with the rapidly overwhelming number of simultaneously critical patients drew the conversion of the majority of neurological units into non-specialistic wards for broader and generic COVID-19 patient care. The converted units became spokes referring neurological patients to tertiary hub centres for specialty care. This led to the definition in tertiary centres of dedicated medical and nurse teams working in special neuro-COVID units in order to guarantee equal access to acute therapies.

The aim of this study was to investigate the impact of COVID-19 by recording clinical presentations, laboratory characteristics and management/outcomes of a series of neurological patients who consecutively presented at the emergency department (ED) during the peak of the epidemic. The study was carried out in a tertiary referral neurological centre, the first Italian neuro-COVID unit, identified as a hub for stroke and neurological emergencies independently from SARS-CoV-2 status, in an area of more than 1 200 000 people.[1]

RESULTS

Five hundred and five adult patients with neurological symptoms were evaluated at the ED starting from 20 February to 30 April 2020. Of these, 147 (29.1%) were found positive for SARS-CoV-2 (table 1).

Compared with patients without COVID-19, COVID-19-positive patients were significantly older (73.1±12.4 vs 65.1±18.9 years, p=0.001) and had a different distribution of neurological presentation (p=0.001), with a higher frequency of altered mental status or delirium (25.9% vs 10.1%) but lower frequency of seizures and headache/pain (see table 1 for details). According to final diagnosis, COVID-19-positive patients had higher prevalence of ischaemic stroke (n=51, 34.7% vs n=105, 29.3%), delirium (n=24, 16.3% vs n=18, 5.0%) and meningitis/encephalitis (n=14, 9.5% vs n=7, 1.9%) (online supplemental table 1 and online supplemental figure 1)

Laboratory analysis in COVID-19-positive patients showed increased serological levels of C reactive protein, aspartate and alanine aminotransferase and fibrinogen (all p<0.05, table 1).

COVID-19-positive patients showed a higher rate of hospitalisation following ED triage (91.2% vs 69.3%, p<0.0001) and in-hospital mortality (29.7% vs 3.1%, p<0.0001). In particular, mortality was higher in intracerebral haemorrhage (ICH) (COVID-19-positive 58.3% vs non-COVID-19 33.0%), in ischaemic stroke (COVID-19-positive 39.2% vs non-COVID 2.8%) and in delirium/altered mental status (COVID-19-positive 23.4% vs non-COVID 0%). In COVID-19, mortality was associated with older age and comorbidities.

According to the Modified Rankin Scale, COVID-19-positive patients had higher levels of disability at discharge compared with patients without COVID-19 (2.6 ±1.6 vs 1.6±1.4, p<0.0001), though both groups had similar baseline values (table 1).

DISCUSSION

Findings showed that about a third of neurological patients assessed at the ED were positive for SARS-CoV-2 and that these were characterised by an increased frequency of cerebrovascular events and encephalitis (online supplemental figure 1). The higher frequency of cerebrovascular events is in line with the known proinflammatory state associated with increased risk of both ischaemic stroke and ICH. In fact, in this series, neurological patients with COVID-19 showed significantly higher levels of C reactive protein and fibrinogen, strongly arguing for endothelial dysfunction or cardioembolic events as possible risk factors for cerebrovascular accidents.

Diagnosis of encephalitis was also more frequently observed in patients with COVID-19. Given the close time relationship with SARS-CoV-2 infection, a direct or inflammatory-mediated involvement of COVID-19 of the CNS has been hypothesised to be in agreement with several case descriptions.

In this series, neurological patients with COVID-19 had an unfavourable outcome as shown by increased rates of hospitalisation, high rate of mortality and higher disability at discharge. The mortality rate observed is far higher compared with general in-hospital mortality reported in COVID-19 both in China and in Western countries,[4] and is higher compared with non-COVID-19 cases also adjusting for age and comorbidities. This further highlights the severe impact of COVID-19 on neurological patients, with these patients being more fragile, vulnerable and thus particularly prone to early deterioration and death independently from age and premorbid state.

This study, evaluating more than 500 patients admitted at the ED, highlighted the fact that COVID-19 infection specifically affects clinical presentations and management of neurological patients. This has deep implications for daily practice and healthcare organisation. For neurological patients severe enough to warrant hospitalisation, our experience suggests that the neuro-COVID units might represent the most suitable solution to provide urgent, standardised and tailored neurological care.[5]

We acknowledge that this study entails some limitations. First, due to the study design, we limited the observation to patients presenting with prominent neurological manifestations, thus probably underestimating neurological symptoms in more severe patients. Second, interpretation of findings could be limited by the single-centre design and by the redistribution of emergency network in the region, potentially leading to decreased access to healthcare systems for less severe neurological manifestations. Third, the study was descriptive in nature and does not include a detailed description of cerebrospinal fluid analyses or MRI imaging, which was not performed as standard in all patients, and perspective studies using standardised protocols are thus warranted to extend these findings.[3]

Table 1 Demographic, clinical, laboratory characteristics and clinical management of neurological patients evaluated at the ED

	Total (N=505)	non-COVID-19 (n=358)	COVID-19 (n=147)	P value
Demographic and clinical characteristics				
Age (years)	64.4±17.6	65.1±18.9	73.1±12.4	<0.0001
Sex				0.92
Female	255 (50.5%)	180 (50.3%)	75 (51.0%)	
Male	250 (49.5%)	178 (49.7%)	72 (49.0%)	
Comorbidities				
Hypertension	290 (57.4%)	216 (60%)	74 (50.9%)	0.09
Diabetes	97 (19.2%)	62 (17.3%)	35 (23.8%)	0.08
Coronary heart disease	62 (12.3%)	40 (11.2%)	22 (15.2%)	0.31
Chronic kidney disease	21 (4.1%)	16 (4.5%)	5 (3.5%)	0.79
Malignancy	96 (19.0%)	75 (20.9%)	21 (14.3%)	0.12
Main clinical presentation				
Acute feature/symptoms	285 (56.4%)	203 (56.7%)	82 (55.8%)	0.001
Subacute/chronic feature/symptoms	39 (7.7%)	31 (8.7%)	8 (5.5%)	
Seizure	54 (10.7%)	44 (12.3%)	10 (6.8%)	
Altered mental state/agitation	74 (14.7%)	36 (10.1%)	38 (25.9%)	
Loss of consciousness	21 (4.2%)	14 (3.9%)	7 (4.8%)	
Headache/pain	32 (6.3%)	30 (8.4%)	2 (1.4%)	
Laboratory findings at ED				
White cell count (mm^3)	8.9±4.8	8.6±3.2	9.5±7.3	0.07
Lymphocytes count (mm^3)	1.6±1.1	1.6±0.8	1.6±1.4	0.23
Platelet count per (mm^3)	249.7±96.4	252.6±92.1	243.1±105.7	0.32
Haemoglobin (g/L)	134±17	135±16	131±18	0.05
C reactive protein (mg/L)	19.5±41.2	12.8±31.9	34.4±53.7	**<0.0001**
Alanine aminotransferase (U/L)	30.5±31.4	27.07±25.1	36.7±41.7	**0.008**
Aspartate aminotransferase (U/L)	30.4±31.5	28.1±31.2	35.5±31.8	**0.04**
Fibrinogen (mg/dL)	363.1±138.7	339.7±122.5	408.7±157.1	**0.001**
Management and outcomes				
Hospitalisation rate	382 (75.6%)	248 (69.3%)	134 (91.2%)	**<0.001**
Modified Rankin Scale, preadmission	1.1±1.3	1.16±1.3	0.9±1.0	0.82
Modified Rankin Scale, discharge	1.9±1.5	1.6±1.4	2.6±1.6	**<0.001**
In-hospital mortality	53 (10.7%)	11 (3.1%)	43 (29.7%)	**<0.001**

Data are mean or n (%). P values were calculated by t-test or Fisher's exact test, as appropriate.
Significant comparisons are highlighted as boldfaced p value
ED, emergency department.

In conclusion, coronavirus plays a relevant impact on neurological presentations and health status, as neurological patients required more frequent hospitalisation and were at higher risk of mortality and disability at discharge. Further studies are needed to compare different models of care in order to identify the most efficacious organisation to counteract the impact of COVID-19 on neurological patients.

Andrea Pilotto [1,2] **Alberto Benussi** [1] **Ilenia Libri,**[1] **Stefano Masciocchi,**[1] **Loris Poli,**[1] **Enrico Premi,**[3] **Antonella Alberici,**[1] **Enrico Baldelli,**[1] **Sonia Bonacina,**[1] **Laura Brambilla,**[4] **Matteo Benini,**[5] **Salvatore Caratozzolo,**[1] **Matteo Cortinovis,**[1] **Angelo Costa,**[3] **Stefano Cotti Piccinelli** [1] **Elisabetta Cottini,**[1] **Viviana Cristillo,**[1] **Ilenia Delrio,**[3] **Massimiliano Filosto,**[1] **Massimo Gamba,**[3] **Stefano Gazzina,**[6] **Nicola Gilberti,**[3] **Stefano Gipponi,**[1] **Marcello Giunta,**[1] **Alberto Imarisio,**[1] **Paolo Liberini,**[1] **Martina Locatelli,**[1] **Francesca Schiano,**[1] **Ranata Rao,**[1] **Barbara Risi,**[1] **Luca Rozzini,**[1] **Andrea Scalvini,**[1] **Veronica Vergani,**[3] **Irene Volonghi,**[1] **Nicola Zoppi** [1] **Barbara Borroni** [1] **Mauro Magoni,**[3] **Matilde Leonardi,**[7] **Gianluigi Zanusso,**[8] **Sergio Ferrari** [8] **Sara Mariotto** [8] **Alessandro Pezzini,**[1] **Roberto Gasparotti,**[9] **Ciro Paolillo,**[10] **Alessandro Padovani**[1]

[1]Neurology Unit, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy
[2]Parkinson's Disease Rehabilitation Centre, FERB Onlus, Trescore Balneario, Lombardia, Italy
[3]Stroke Unit, ASST Spedali Civili di Brescia, Brescia, Italy
[4]Department of Neuroimmunology and Neuromuscular Diseases, Foundation IRCCS Carlo Besta Neurological Institute, Milano, Italy
[5]Neurology Unit, University of Bologna, Bologna, Italy
[6]Neurophysiology Unit, ASST Spedali Civili di Brescia, Brescia, Italy
[7]Neurology, Public Health and Disability Unit, Foundation IRCCS Carlo Besta Neurological Institute, Milano, Italy
[8]Department of Neuroscience, Biomedicine and Movement Sciences, University of Verona, Verona, Italy
[9]Section of Neuroradiology, Department of Medical and Surgical Specialties, University of Brescia, Brescia, Italy
[10]Emergency Department, ASST Spedali Civili di Brescia, Brescia, Italy

Correspondence to Professor Alessandro Padovani, Department of Clinical and Experimental Sciences, University of Brescia, 25121 Brescia, Italy; alessandro.padovani@unibs.it

Twitter Roberto Gasparotti @bobgas@giumbomix

Contributors Conception and design of the study: APi, AB and APe. Acquisition and analysis of data: APi, AB, IL, SM, LP, EP, APe, EB, SB, LB, MB, SC, MC, AC, SCP, EC, VC, ID, MF, MG, SGa, NG, SGi, MG, AI, PL, MLo, FS, RR, BR, LR, AS, VV, IV, NZ, BB, MM, MLe, GZ, SF, SM, APa, RB, CP and AP. Drafting of the manuscript and figures: APi, AB and APe.

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ORCID iDs
Andrea Pilotto http://orcid.org/0000-0003-2029-6606
Alberto Benussi http://orcid.org/0000-0002-8703-6940
Stefano Cotti Piccinelli http://orcid.org/0000-0002-2060-0279
Nicola Zoppi http://orcid.org/0000-0002-6594-0517
Barbara Borroni http://orcid.org/0000-0001-9340-9814
Sergio Ferrari http://orcid.org/0000-0003-3855-5135
Sara Mariotto http://orcid.org/0000-0002-7806-3103

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