

INITIAL NEUROLOGICAL SYMPTOMS ASSOCIATED WITH COVID-19 DURING THE FIRST OUTBREAK IN BULGARIA

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Abstract

During the first outbreak of COVID-19 in the spring of 2020 different symptoms of the disease were reported. Therefore, this study aimed to evaluate initial neurological symptoms of COVID-19 among hospitalized patients in that time period.

In patients with confirmed COVID-19, initial symptoms, concomitant diseases, neurological signs, and neurological status were assessed.

Sixty-six patients (mean age 63 years) were prospectively enrolled, 44 (66.7%) of them were males. Initial neurological symptoms were reported by 51 (77.3%), most commonly headache (14 [21.2%]), dizziness, and vertigo (14 [21.2%]). Dysgeusia was present in 13 (19.7%) and anosmia in 10 (15.2%) patients. Initial neurological symptoms were observed in 20 (76.9%) of ≤ 60 years patients, and 31 (77.5%) of > 60 years patients. Focal neurological deficit was found in 35 (53%) patients, 11 (42.3%) were ≤ 60 years.

The presence of initial neurological symptoms in this study is higher than previously reported, without a difference in age groups, despite the higher somatic burden in the group of patients over 60 years of age.

Key words: neurological symptoms, COVID-19, Bulgaria

Introduction. The current COVID-19 pandemic has caused a worldwide emergency in the healthcare system [1]. It is caused by a beta coronavirus called

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SARS-CoV-2 which has a strong affinity to the Angiotensin-Converting Enzyme 2 (ACE2), expressed mainly in the lungs, but also in the heart, kidneys and blood vessels [2]. For that reason, apart from its most dramatic complication, the severe acute respiratory distress syndrome (SARS), may be responsible for a couple of symptoms including neurological manifestations. The experience with the previous two coronavirus epidemics, namely with SARS in 2002 and especially with MERS in 2012 shows in some cases a neurological involvement. This includes ischemic stroke [3], epileptic seizures [4], but also impaired consciousness and ataxia [5], or intracerebral hemorrhage [6]. However, the evidence about initial focal and/or global deficits due to impaired function of the central and peripheral nervous system is still insufficient, especially in the countries of southeastern Europe like Bulgaria, which recently report a dramatic escalation of confirmed COVID-19 cases. Therefore, this study aims to describe neurological manifestations in the initial phase of the COVID-19.

Materials and methods. Study sample. In this prospective cross-sectional study, we included 66 patients with diagnosed COVID-19, which were admitted, diagnosed, and treated in two university hospitals (Pirogov University Hospital, St. Anna University Hospital) and one district hospital (Second Multi-profile Hospital). These were tertiary referral centres for COVID-19 in the region of Sofia – the area with the highest density of COVID-19 cases. Patients were recruited predominantly in Pirogov University Hospital. All patients were examined between April 1st and May 15th 2020. To estimate age as a factor, patients were grouped in under and over 60 years.

Study protocol and procedures. All enrolled patients had a confirmed COVID-19, based on clinical and laboratory criteria. Informed consent was obtained by each participant or by his/her relative. We reviewed patients' history, which included basic demographic data (age and sex) and concomitant diseases. Regarding COVID-19, initial complaints and neurological symptoms were included. A detailed neurological examination was performed in each participant by a board-certified neurologist. The results were categorized into two groups: 1) impaired consciousness, and 2) focal neurological deficit. Because of temporal restraints, questionnaires, or another objective metric was not included.

Statistical analysis. For the statistical analysis, we used IBM SPSS version 23 for Windows. All subjects were described using descriptive statistics and frequency analysis. A p value of ≤ 0.05 was set as statistically significant. Scale variables were calculated as mean, median, and standard deviation. A Chi-square test was used for the comparison of categorical frequencies. Parametric and non-parametric tests were implemented for the independent sample group comparison.

Results. In this study, we included 66 hospitalized patients with confirmed SARS-CoV-2, forty-four (66.7%) were males. The mean age was 63 years and median of 67 years (range 24–95 years). Fifty-three (80.3%) patients had at least one underlying disorder. Arterial hypertension was the most common one (41

[62.1%]), followed by diabetes mellitus (13 [19.7%]), coronary heart disease (12 [18.2%]), congestive heart failure (9 [13.6]), malignant neoplasm (7 [10.6]), and chronic obstructive pulmonary disease (5 [7.6]).

The most common initial symptoms of COVID-19 were fever (51 [77.3%]), cough 49 (74.2%), dyspnea (43 [65.2%]), fatigue (39 [59.1]), and muscle pain (16 [24.2]). The clinical course of COVID-19 presented with improvement in 33 (50%), stability in 25 (37.9%), and with worsening in 7 (10.6%) patients.

Initial neurological symptoms were reported by 51 (77.3%). Their description is summarized in Table 1.

T a b l e 1
Initial neurological symptoms in patients, diagnosed with COVID-19

Neurological symptom	N	%
Headache	14	21.2
Impaired consciousness	9	13.6
Disorientation	10	15.2
Dizziness and vertigo	14	21.2
Balance instability	9	13.6
Dysgeusia	13	19.7
Anosmia	10	15.2
Dysphonia	9	13.6
Dysarthria	4	6.1
Dysphagia	2	3
Tremor	2	3

In the group analysis, 40 (60.6 %) participants were over 60 years of age. The gender distribution was with male predominance in both groups – 19 (73.1%) males in those under and equal to 60 years, and 25 (62.5%) males in patients > 60 years. The clinical course in the ≤ 60 years group was 17 (65.4%) improvement, 6 (23.1%) stable, and 3 (11.5%) worsening. In the group over sixty years the distribution was as follows: 16 (40%) improvement, 19 (47.5%) stable, and 4 (10%) worsening.

The group distribution of initial neurological symptoms is depicted in Fig. 1. They were present in 20 (76.9%) of ≤ 60 years patients, and 31 (77.5%) of > 60 years patients. Impaired consciousness was observed in 14 (21.2%), where 5 (19.2%) were ≤ 60 years. Focal neurological deficit was found in 35 (53%) patients, 11 (42.3%) were ≤ 60 years.

Discussion. In this study, we included prospectively patients with confirmed COVID-19 for initial neurological symptoms during the first disease outbreak in Bulgaria. The mean age (63 years) and the male predominance correspond with the overall demography of COVID-19 [7]. From the comorbidities, the cardiovascular burden was the highest, which given the mean age, was expected. Of them,

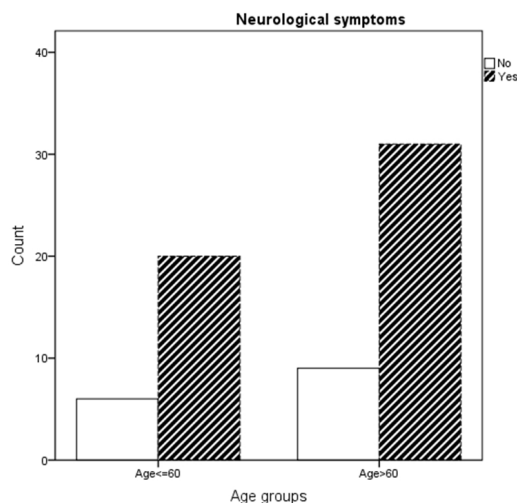


Fig. 1. Group presentation of the initial neurological symptoms

arterial hypertension was found to be the most common underlying disorder, with twice higher prevalence than reported [8]. In our study however, the average age of the patients was higher.

As the most common COVID-19 onset symptoms we identified fever, cough, dyspnea, fatigue, and muscle pain, which is in accordance with other studies [9]. The disease course was in general favourable, with clinical improvement or stability in over 90% of participants. This finding is more optimistic than in previous reports [10], nevertheless, in the current study, the main focus was not the COVID-19 burden.

We found initial neurological symptoms in over 2/3 of our patients which is significantly higher than reported by MAO et al. [11]. This is evident in the unspecific complaints such as headache, dizziness, and vertigo, but also some more specific symptoms – dysgeusia and anosmia [12]. Moreover, we found focal and/or global neurological deficit in over 62% of our patients. Since there is still an insufficient number of similar studies, we cannot draw any solid conclusion yet. Nevertheless, the neurological focus of this study could be an important reason for our findings. However, other contributing factors could be the population differences, older age of patients, or distinctive underlying diseases, with an impact on the initial somatic and neurologic burden before developing COVID-19. This in our opinion confirms the need for a thorough neurological assessment of each COVID-19 patient, even if this might require additional logistical effort, which appears to have increasing acceptance [13, 14].

Given the demographical characteristics of COVID-19 [10], we found 60 years of age a reasonable cutoff, to differentiate “younger” from older “patients”. In this

group analysis, we did not observe any significant demographical differences. The clinical course of COVID-19 was slightly more favourable in the participants under sixty years of age, which might be also due to the lower burden of concomitant diseases. Neurological symptoms shares were almost identical in either group, despite the higher rate of cardiovascular and to some extent cerebrovascular rate in the “older” patients.

Limitations. There are certain limitations to this study. We analyzed only 66 hospitalized patients with COVID-19; therefore, we cannot extrapolate our results over the entire population. The relatively low number of included patients was mainly due to the logistically complicated process of assessment under COVID-19 conditions which was especially prominent during the first disease outbreak in Bulgaria. Since there are still not enough studies on this topic, we could not make a good comparison in terms of the reliability of our data. In this study, we evaluated only initial neurological symptoms, but we did not assess them, concerning possible direct and/or indirect neurological complications.

Conclusions. This is to our knowledge the first study, exploring initial neurological symptoms in COVID-19 in Bulgaria during the first disease outbreak in the spring of 2020. Our results show a relatively high percentage of onset neurological manifestation which confirms the need for thorough neurological evaluation in such patients. Nevertheless, there are still not enough data to draw more robust conclusions. Therefore, further studies on this topic are warranted, which will clarify and corroborate our clinical experience.

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