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The impact of home quarantine during COVID-19 lockdown on neurological hospitalizations, in-hospital mortality, and acute ischemic stroke management in older patients without COVID-19

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ABSTRACT

Introduction: This study aimed to investigate the impact of home quarantine in older patients without COVID-19 hospitalized due to neurological disorders.

Methods: We consecutively enrolled 255 elderly patients(median age: 75 years, female: 54%), including 180 (70%) in the pre-home quarantine period and 75 (30%) home quarantine period from January to May 2020 (ten weeks before and ten weeks after the March 21, 2020, lockdown for older patients in Turkey) in a tertiary referral neurological center.

Results: In the home quarantine period, we documented a fall in the number of neurological admissions by 58.3%, but an increased need for intensive care in older patients. Patients in the home quarantine period were younger [73 (65−91) vs 76 (65−95), $p = 0.005$], had worse Glasgow Coma Scores (12.3 ± 3.6 vs 13.7 ± 2.5, $p = 0.007$), higher in-hospital mortality rate (21.3% vs. 6.7%, $p = 0.001$), had a lower prevalence of comorbidities such as diabetes mellitus, hypertension, and cardiovascular disease, and chronic neurologic disease, albeit had a higher prevalence of the acute cerebrovascular disease (hemorrhagic/ ischemic stroke)(90.7% vs 78.9, $p = 0.025$). In this period, even there was an increase in the proportion of the patients undergoing reperfusion therapy, it wasn't statistically significant (20.3% vs. 10.1%, p: 0.054). Multivariate analysis revealed that high NIHSS (The National Institutes of Health Stroke Scale) score (OR=1.25; $p < 0.001$) and hospitalization in the home quarantine period (OR=3.21; $p = 0.043$) were independently associated with in-hospital mortality.

Conclusion: Our study indicated that during the COVID-19 home quarantine period, despite a significantly fewer number of patients admitted to the hospitalization, there was a higher percentage of those hospitalized needing intensive care and an overall worse prognosis.

1. Introduction

After Turkey reported its first COVID-19 case on March 10, 2020, and a week later, the first COVID-19-related death; On March 21, 2020, a partial curfew was imposed for citizens aged 65 years and older in the scope of COVID-19 measures, and they were ordered to stay at home [1, 2]. In a short time, The Republic of Turkey implemented several healthcare system measures, e.g., elective procedures were postponed, only the urgent ones were permitted, access to healthcare services, especially for emergencies, was provided [3]. Planned hospital admissions and outpatient visits are either limited or canceled. Worldwide, as a result of all the measures and regulations taken, a decrease in both general and geriatric admissions to emergency services, and neurological admissions were reported [4–6], and a significant decrease was observed in the number of patients admitted for reasons such as acute stroke and acute coronary syndrome [7]. By the end of May 2020, The government considered easing the restrictions imposed on the movement of those aged over 65 [8].

Neurological problems are one of the most common reasons for geriatric patients admitting to emergency services and hospitalization.

Abbreviations: Covid 19, Coronavirus Disease 2019.

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In older individuals with neurological symptoms, a delay in diagnosis and lack of the appropriate treatment can lead to rapid deterioration, sequelae, and death.

In the era of the current COVID-19 health crisis, many publications in neurology mainly focused on the effect of the pandemic on the emergency admissions of patients with neurological symptoms, and neurological symptoms, manifestations, and complications of patients with COVID-19 [9–11]. There are scarce published data on how social isolation affects neurological hospitalizations in the home quarantine period in older patients without COVID-19. Therefore, we herein aimed to investigate the influence of the home quarantine on neurological-related hospitalization rates, acute ischemic stroke management, and in-hospital mortality during the home quarantine period in older patients without COVID-19.

2. Material and methods

This study was conducted in a tertiary referral hospital (Bursa City Hospital) with a comprehensive stroke center covered by common stroke and neuro-interventional teams, offering reperfusion therapy [intravenous thrombolysis (IVT) and mechanical thrombectomy (MT)]. All consecutive admissions to the neurological services and intensive care unit throughout 10-weeks prior and 10-weeks during the COVID-19 home quarantine period, namely between 13 January to 21 March 2020, and 22 March to 29 May 2020, were retrospectively analyzed. We excluded patients younger than 65 years and diagnosed with COVID-19 having either positive reverse transcriptase-polymerase chain reaction assay for SARS-CoV-2 in a nasopharyngeal swab or a chest X-ray or CT scan showing the characteristic interstitial pneumonia of COVID-19. Of 457 neurological cases hospitalized in either neurological services or intensive care unit during the study period, 255 met the inclusion criteria (Fig. 1).

These sociodemographic and clinical variables were collected from a review of electronic records:

1. Demographics (age, sex, admission date, and time)
2. Neurological comorbidities, including cerebrovascular accident (CVA), Parkinson's Disease, dementia, epilepsy, motor neuron disease, multiple sclerosis
3. Hospitalization place and duration
4. Pulmonary and cardiovascular comorbidities, including hypertension, diabetes mellitus, chronic obstructive pulmonary disease (COPD), asthma
5. Acute cerebrovascular disease, including transient ischemic attack, hemorrhagic or ischemic CVA
6. Patients receiving reperfusion therapy
7. In-hospital death

At admission, patients' consciousness for all and stroke severity for acute stroke patients were evaluated using the Glasgow Coma Scale (GCS) and National Institutes of Health Stroke Scale (NIHSS) scores, respectively. The study was approved by the ethics committee of our institution (Number: 2021–7/18, Date:21.04.2021) and was carried out in accordance with the Declaration of Helsinki.

2.1. Statistical analyses

Statistical package for the social sciences (SPSS) version 21.0 was used for statistical analyses. Continuous variables were assessed by Kolmogorov-Smirnov test and histograms to find out if they had normal or skewed distribution. Normally distributed parameters were compared by the Student T-test and others by the Mann-Whitney *U* test. Categorical variables were compared by Chi-square or Fisher Exact tests, where appropriate. Categorical variables were presented as number and frequency. P-value < 0.05 was considered statistically significant. Multivariate binary logistic regression was used to identify independent predictors associated with in-hospital mortality. Variables that remained significant ($p < 0.05$) in the multivariate model were considered as independent predictors for in-hospital mortality. Hosmer-Lemeshow goodness of fit statistics was performed to assess model fit. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for each predictor. All variables in Table 2 were determined by clinical significance and tested for multicollinearity; variables with $P < 0.2$ after univariate analysis were entered into the multivariable logistic regression model. The final models were determined by backward elimination procedures with $P < 0.05$ as model retention criteria. Finally, the following confounders, determined by clinical significance and multicollinearity, were entered into the multivariate model: Age, gender, NIHSS score, hospitalization period, admission time to the hospital, presence of hypertension, presence of diabetes mellitus, acute cerebrovascular disease (hemorrhagic or ischemic), and malignity.

3. Results

Between January 13 and May 29, 2020 (i.e., ten weeks before and ten weeks after the March 21, 2020, lockdown for older patients in Turkey),

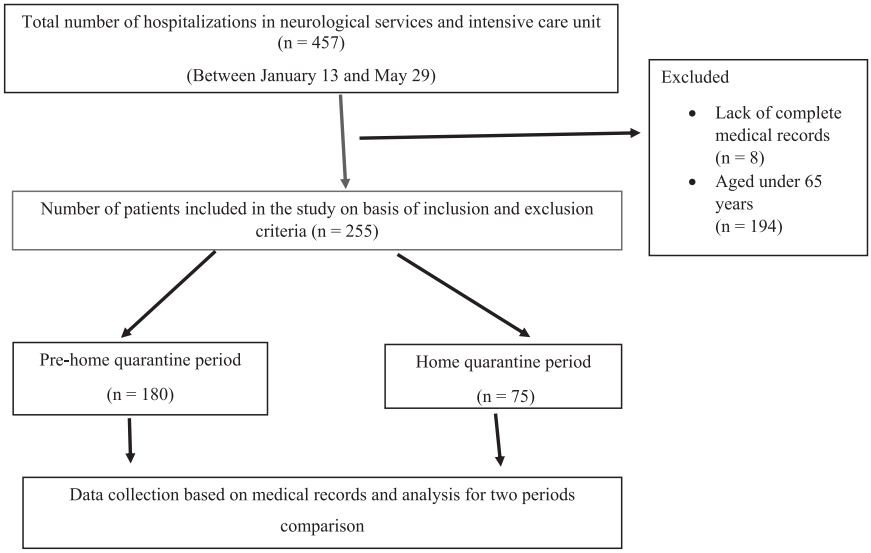

Fig. 1. Flow diagram for this study.

255 older patients were consecutively admitted to the neurology clinic and intensive care unit. The median age of the participants was 75 (range 65–95), and gender distributions were similar between the two groups. Patients in the home quarantine period were younger [73 (65−91) vs. 76 (65−95)], the proportion of those aged 75 and over was lower in this group when patients were categorized into two groups as 65–75 years, and 76 and over (32% vs. 55%). Of patients, 75 were admitted during the home quarantine period, and there is an increase in patients needing intensive care hospitalization in this period.

The admittance diagnoses, sociodemographic, and clinical characteristics of the included patients are displayed in Table 1. While patients in the home quarantine period had a lower prevalence of comorbidities such as diabetes mellitus, hypertension, cardiovascular disease, and chronic neurologic disease, they had a higher prevalence of acute cerebrovascular disease (90.7% vs. 78.9%, p: 0.025). Patients in the home quarantine period had worse neurologic deficits than those in the pre-home quarantine period. Glasgow Coma Scores (GCS) were lower in both the initial admission and patients diagnosed with acute cerebrovascular disease in the home quarantine period [12.3 ± 3.6 vs.13.7 ± 2.5 (p = 0.007) and 12.3 ± 3.6 vs. 13.4 ± 2.7 (p = 0.031), respectively]. The mortality rate was higher in the home quarantine period (21.3% (n = 16) vs. 6.7% (n = 12), p: 0.001). Cerebral herniation was the leading cause of death, followed by multiorgan failure and sepsis (Table 1). Furthermore, findings suggest that older age, being followed up in intensive care unit, admittance to the emergency department between 19:00 and 07:00, high NIHSS, and low GCS conferred an increased risk of mortality among older patients. The results of the study regarding mortality are presented in Table 2. Concerning gender differences in stroke patients (hemorrhagic or ischemic), women were older and had a higher NIHSS score and an in-hospital death rate (Table 3).

There was an increase in the proportion of patients undergoing reperfusion therapy due to acute stroke in the home quarantine period, arbeit it doesn't reach any statistical significance (20.3% vs. 10.1%, p: 0.054). Age, gender distribution, duration of hospitalization, the time from symptoms onset to arrival to the hospital, the time of reperfusion treatment (door-to-needle and door-to-puncture), the NIHSS score upon hospital arrival of these patients, however, did not differ between two periods.

A binary logistic regression analysis was performed to detect the possible parameters that affect in-hospital mortality. Multivariate analysis revealed that high NIHSS (The National Institutes of Health Stroke Scale) score (OR=1.25, 95% CI:1.16–1.35; p < 0.001) and hospitalization in the home quarantine period (OR=3.21, 95% CI:1.04–9.95; p = 0.043) were independently associated with in-

Table 1
Baseline characteristics of the patients.

	Pre-home Quarantine (n = 180)	Home Quarantine (n = 75)	p
Age, median (min-max)	76 (65–95)	73 (65–91)	**0.005**
Age			**0.001**
– Between 65 and 75 years, n (%)	81 (45)	51 (68)	
– 76 years and over, n (%)	99 (55)	24 (32)	
Female, n (%)	91 (50.6)	47 (62.7)	0.077
Hospitalization			**< 0.001**
1. In neurology clinic, n (%)	145 (80.6)	39 (52)	
2. In the neurology intensive care unit, n (%)	35 (19.4)	36 (48)	
Duration of hospitalization, median (min-max)	6 (1–205)	8 (1–165)	0.159
Glasgow coma score, median (min-max)			
1. All patients	13.7 ± 2.5	12.3 ± 3.6	**0.007**
2. Patients with acute hemorrhagic or ischemic CVA	13.4 ± 2.7	12.3 ± 3.6	**0.031**
Admission time			0.250
– Between 19:00 – 07:00, n (%)	70 (38.9)	35 (46.7)	
– Between 07:00 – 19:00, n (%)	110 (61.1)	40 (53.3)	
In Hospital Mortality, n (%)	12 (6.7)	16 (21.3)	**0.001**
In Hospital Death			**0.377**
1. Cerebral herniation, n (%)	2 (16.7)	6 (37.5)	
2. Lower respiratory tract infection, n (%)	3 (25)	1 (6.3)	
3. Sepsis, n (%)	3 (25)	2 (12.5)	
4. Myocardial infarction or sudden death, n (%)	1 (8.3)	1 (6.3)	
5. Multiorgan failure, n (%)	1 (8.3)	0 (0)	
6. Metabolic coma, n (%)	1 (8.3)	1 (6.3)	
7. Unknown cause, n (%)			
Acute CVA (hemorrhagic or *ischemic*), n (%)	142 (78.9)	68 (90.7)	**0.025**
Stroke subtype			
1. Hemorrhagic stroke	13 (8)	9 (12.7)	0.216
2. Ischemic stroke	129 (79.6)	59 (83.1)	0.247
3. TIA, n (%)	20 (12.3)	3 (4.2)	0.071
Chronic neurological disease[a], n (%)	49 (27.2)	11 (14.7)	**0.031**
Epilepsy (newly diagnosed), n (%)	7 (3.9)	0 (0)	0.109
Hypertension, n (%)	101 (56.1)	29 (38.7)	**0.011**
Diabetes Mellitus, n (%)	52 (28.9)	11 (14.7)	**0.016**
Cardiovascular Disease, n (%)	50 (27.8)	10 (13.3)	**0.013**
Chronic Kidney Disease, n (%)	8 (4.4)	3 (4)	0.874
Malignity, n (%)	1 (0.6)	3 (4.1)	0.074
Chronic Obstructive Pulmonary Disease, n (%)	9 (5)	2 (2.7)	0.519

Abbreviations: CVA, Cerebrovascular accident; TIA, Transient ischemic attack

[a] Chronic neurological disease refers to the sum of the patients with a history of CVA, Parkinson's disease, dementia, epilepsy, motor neuron disease, multiple sclerosis.

Table 2
The results of the study regarding mortality.

	In Hospital Mortality		
	No (n = 227)	Yes (n = 28)	p
Age, median (min-max)	75 (65–95)	79 (67–90)	0.086
Age, 76 years and over, n (%)	106 (46.7)	17 (60.7)	0.161
Female, n (%)	119 (52.4)	19 (67.9)	0.122
Glasgow coma score, median (min-max)	15 (3–15)	8 (3–15)	**< 0.001**
NIHSS, median (min-max)	4 (1–26)	21 (4–28)	**< 0.001**
Hospitalization in intensive care unit, n (%)	47 (20.7)	24 (85.7)	**< 0.001**
Home quarantine period, n (%)	59 (26)	16 (57.1)	**0.001**
Reperfusion therapy in home quarantine period, n (%)	9 (47.4)	3 (50)	0.910
Admission between 19:00 and 07:00, n (%)	88 (38.8)	17 (60.7)	**0.026**
TIA, n (%)	24 (10.6)	0 (0)	0.087
Acute CVA (hemorrhagic *or* ischemic), n (%)	184 (81.1)	26 (92.9)	0.186
Chronic neurological disease[a], n (%)	51 (22.5)	9 (32.1)	0.255
Hypertension, n (%)	121 (53.3)	9 (32.1)	**0.035**
Diabetes Mellitus, n (%)	63 (27.8)	0 (0)	**0.001**
Epilepsy newly diagnosed, n (%)	6 (2.6)	1 (3.6)	0.562
Cardiovascular Disease, n (%)	53 (23.3)	7 (25)	0.846
Chronic Kidney Disease, n (%)	9 (4)	2 (7.1)	0.345
Malignity, n (%)	2 (0.9)	2 (7.1)	0.062
Chronic Obstructive Pulmonary Disease, n (%)	10 (4.4)	1 (3.8)	0.895

Abbreviations: NIHSS, The National Institutes of Health Stroke Scale; TIA, Transient ischemic attack

[a] Chronic neurological disease refers to the sum of the patients with a history of CVA, Parkinson's disease, dementia, epilepsy, motor neuron disease, multiple sclerosis.

Table 3
Clinical data in men and women with stroke.

	Men (n = 95)	Women (n = 115)	p
Age, median (min-max)	73 (65–93)	76 (65–95)	**0.034**
Hospitalization			0.061
1. In neurology clinic, n (%)	71 (74.7)	72 (62.6)	
2. In the neurology intensive care unit, n (%)	24 (25.3)	43 (37.4)	
Duration of hospitalization, median (min-max)	8 (1–205)	7 (1–108)	0.385
Glasgow coma score, median (min-max)	15 (3–15)	15 (3–15)	0.097
NIHSS, median (min-max)	4 (1–27)	5 (1–28)	**0.032**
In-hospital mortality, n (%)	7 (7.4)	19 (16.5)	**0.045**
Chronic neurological disease[a], n (%)	18 (18.9)	29 (25.2)	0.278
Hypertension, n (%)	47 (49.5)	64 (55.7)	0.372
Diabetes Mellitus, n (%)	17 (17.9)	30 (26.1)	0.156
Cardiovascular Disease, n (%)	21 (22.1)	28 (24.3)	0.702
Chronic Kidney Disease, n (%)	4 (4.2)	5 (4.3)	0.961
Stroke subtypes			
1. Ischemic stroke	82 (86.3)	106 (92.2)	0.168
2. Hemorrhagic stroke	13 (13.7)	9 (7.8)	0.168
Malignity, n (%)	0 (0)	3 (2.6)	0.256

Abbrevations: NIHSS, The National Institutes of Health Stroke Scale
[a] Chronic neurological disease refers to the sum of the patients with a history of CVA, Parkinson's disease, dementia, epilepsy, motor neuron disease, multiple sclerosis.

hospital mortality after adjustment for age, gender, NIHSS score, hospitalization period, admission time to the hospital, presence of hypertension, presence of diabetes mellitus, acute cerebrovascular disease (hemorrhagic or ischemic), and malignity. The results of logistic regression analysis are summarized in Table 4.

4. Discussion

To the authors' knowledge, this is the first study to assess the impact of COVID-19 home quarantine on the provision of neurological services and an intensive care unit together with in-hospital mortality in older patients without COVID-19.

Given the results of the study, the causes for the decrease in hospitalizations may likely be multifactorial and include patient reluctancy of hospital admission for fear of COVID-19, changes in patient lifestyle in the context of social distancing, the possibility of opting for outpatient treatment instead of hospitalization for relatively mild cases, redeployment of neurologists to COVID-19 units, and the reduced number of beds in the neurology services. In addition, there is a possibility that neurological symptoms may be overlooked as elderly patients living alone cannot be visited frequently by their families who are their primary point of contact for recognition of changes in health status and ensure transportation to access medical care visits during this period. Besides these, patients may have preferred to go to another hospital as our hospital is a pandemic hospital. Another reason for the decline in hospitalization may be that in our study we excluded patients with COVID-19, some patients admitted and diagnosed with COVID-19 may have also been managed for neurological problems and hospitalized in COVID-19 units.

Table 4
Independent predictors of in-hospital mortality.

	Unadjusted		Adjusted	
Risk Factors	OR (95% CI)	p	OR (95% CI)	p
NIHSS score	1.24 (1.16–1.34)	**< 0.001**	1.25 (1.16–1.35)	**< 0.001**
Hospitalization in home quarantine period	3.80 (1.70–8.49)	**0.001**	3.21 (1.04–9.95)	**0.043**

Abbrevations: NIHSS, The National Institutes of Health Stroke Scale
The p-value of the Hosmer-Lemeshow test was 0.839, the following factors were entered into the multivariate logistic regression analysis: Age, gender, NIHSS score, hospitalization period, admission time to the hospital, presence of hypertension, presence of hypertension, acute cerebrovascular disease(hemorrhagic or ischemic), and malignity. Area under the ROC curve = 0.930; sensitivity = 92.3%; specificity = 86.4%; positive predictive value = 49%; negative predictive value = 98.8%.

In our study, we found that the clinical picture of hospitalized patients during the home quarantine period was more severe and the in-hospital mortality rate was higher than the pre-quarantine period. Our findings demonstrate and multivariate analysis supports that hospitalizations in home quarantine period is independently associated with in-hospital mortality. Early recognition and intervention, especially for acute cerebrovascular disease, can mitigate deleterious outcomes. Alas, not only enforcement of social distancing measures and quarantines but also aforementioned reasons may contribute to neurological symptoms being discovered late, resulting in morbidity and mortality [12]. These findings support concerns about the negative impact on the acute management of non-COVID-19-related conditions of the current ongoing pandemic. Maintaining continuity of care for patients with chronic diseases or severe acute conditions during the home quarantine period seems to be crucial. Interestingly, in addition to these findings, compared to the pre-home quarantine period, we also observed that geriatric patients hospitalized during the home quarantine were younger, and comorbid diseases such as diabetes mellitus, hypertension, and cardiovascular disease, and the sum of the chronic neurological diseases such as dementia, Parkinson's Disease, epilepsy, amyotrophic lateral sclerosis, multiple sclerosis were accompanied less frequently. It is conceivable that in this period, due to the fear of coronavirus infection frail and older patients with multiple comorbidities and polypharmacy, considering to be the highest risk of contracting the disease may not have been brought to the hospital by their relatives or caregivers, or drug compliance might have been higher in older patients with chronic neurological diseases in this period.

Another key finding is that we found a noteworthy reduction in older patients hospitalized with both hemorrhagic/ischemic stroke and transient ischemic attack. Our results are consistent with published reports from across the world. In a study conducted in a comprehensive tertiary stroke center, D'Anna et al. documented a fall in the number of stroke admissions by 31.33% and of TIA outpatient referrals by 24.44% compared to the same period of the previous year [13]. In an international, observational study a significant global decline was shown in all measured stroke care metrics including the numbers of overall stroke admissions (19.2%), ischemic stroke/TIA admissions (15.1%), and intracranial hemorrhage hospitalization volumes (11.5%) during the COVID-19 pandemic as compared to the preceding three months [14]. We found a nearly 85% decrease in admissions for TIA. Consistent with our study, a decrease in the number of acute ischemic cerebrovascular events admissions most noticeable for TIA was observed [15]. This might be related to the fact that many patients with milder stroke presentations avoid or delay seeking medical attention due to fear of contracting Coronavirus-19 infection. With respect to gender differences in acute stroke patients, we found less favorable outcome in women than in men, with a significantly higher rate of in-hospital death. Our results are in agreement with the study conducted by Arboix et al. [16].

One important point in the current pandemic is related to stroke management. A global decline in the use of intravenous thrombolysis and thrombectomy has been reported [14,17]. It is controversial whether the proportion of patients receiving reperfusion therapy has increased in the COVID-19 pandemic. We found a decrease in the volume but an increase in the proportion of the patients undergoing reperfusion therapy due to acute stroke with borderline significance. Our results align with recent reports emphasizing the effects of the COVID-19 pandemic on stroke management. Saban et al. found an increase in the proportion of patients with acute ischemic stroke who arrived shortly after the onset of symptoms and received timely treatment [18]. Furthermore, in the home quarantine period, we didn't

observe any significant delay to reperfusion for IVT and MT in door-to-needle and door-to-puncture time, respectively. It may be attributable to the preservation of access to reperfusion therapy in the home quarantine period. This finding is in line with other centers [13, 19,20], whereas in apparent conflict with the study conducted by Briard et al. [21]. In an observational cohort study, longer door-to-needle and door-to-recanalization metrics were demonstrated during the COVID-19 pandemic, partly attributed to the institution of infection control measures [21].

Some limitations of the study should be highlighted. The main one is its single-center, retrospective, observational design with a relatively small sample size. Second, the period during the home quarantine could not be analyzed comparatively with the same period of the previous year, since the hospital in which the study was conducted started admitting patients eight months ago before the pandemic. Third, our study was carried out in an area severely hit by the pandemic and may not be representative of other areas with a lower number of COVID-19 cases. These issues may limit the generalizability of our findings to other studies.

The strength of our study is that it is the first single-center study in our country that investigates how older patients, the patient group most affected by the pandemic, were affected by their hospitalization due to neurological symptoms during home quarantine. Even there's hope on the horizon with vaccines and new treatment modalities, the COVID-19 pandemic is still ongoing, and this study is relevant and important during the current pandemic, pointing out the provision of health services for neurological hospitalization without COVID-19.

Hospitalization in the home quarantine period and disease severity (high NIHSS score) at admission were significantly associated with in-hospital mortality due to neurological disorders at our tertiary center. Therefore, a delay in neurological diagnosis of older patients in lockdown period during the pandemic can lead to adverse outcomes and mortality. In conclusion, While taking measures to slow the spread of the infection and calling for ''Stay Home'', it is of utmost importance to inform the public about medical emergencies that require hospital admission. Amidst the pandemic, the greatest challenge seems to be to continue providing care to non COVID individuals. A multicenter, prospective nationwide study with a broader sample size is desirable to confirm our findings.

Disclosure statement

Financial disclosure

None declared.

CRediT authorship contribution statement

Cemile Haki: Conceptualization, Data curation, Investigation, Methodology, Writing – review & editing, Supervision. **Olgun Deniz:** Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing.

Conflicts of interest

None declared.

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