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Examining the effects of COVID-19 pandemic on stroke

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Abstract

The most common neurological disease in the world and one of the leading reasons for mortality is stroke. In addition to its effect on many systems of the body, COVID-19 infection also affects the central nervous system and causes neurological involvement. In our study, we examined the effects of the COVID-19 pandemic on stroke by comparing the pre-pandemic and pandemic times. Patients who presented to the emergency department with a stroke during the same time in two different years were included in the study. Patients with clinical conditions mimicking stroke in the differential diagnosis, those with a positive polymerase chain reaction test for COVID-19, and those with COVID-19 pneumonia were excluded from the sample. Patients diagnosed with stroke were examined using clinical, laboratory, and radiological imaging methods. Length of stay in hospital (service or intensive care unit) and mortality rates were recorded. There was no significant difference between the pre-pandemic and pandemic times in relation to the incidence of ischemic and hemorrhagic stroke, sex, and age. Although the number of patients presenting with an ischemic stroke increased during the pandemic time, the rate of acute ischemic stroke patients decreased. In addition, there was a decrease in the rates of patients who underwent intravenous thrombolytic and mechanical thrombectomy. Stroke cases increased during the pandemic time, but the rate of admission for acute ischemic stroke decreased. Because of this reason patients delaying their hospital visits because of pandemics lost their chance of acute treatment.

Keywords: COVID-19, pandemic, effect, stroke

Introduction

Stroke occurs when a part of the brain is affected as a result of ischemia or bleeding and/or pathological damage to the blood vessel supplying blood to the brain [1]. Stroke is the most common neurological disease in the world and the third main cause of mortality after cardiac diseases and cancer. It also ranks first in terms of causing disability in patients [2]. The World Health Organization defines stroke as a sudden onset, focal or generalized neurological deficit that lasts more than 24 hours and can result in death during this time, in which no other cause other than vascular pathologies can be found [3].

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COVID-19 disease generally progresses with an asymptomatic infection and a process that can be accompanied by mild pneumonia [4]. However, in cases where the infection progresses, respiratory failure may occur, which can sometimes be accompanied by multi-organ failure [5]. In addition to the most common symptoms of fever, cough, fatigue, myalgia, hemoptysis, and shortness of breath, it is known that the infection is not always limited to the respiratory tract, creating problems involving many other systems of the body [6,7]. Studies have shown that this infection may also have neurological involvement [8]. In a study on the COVID-19 pandemic, it was found that neurological signs and symptoms were observed in approximately 36% of patients [9]. Patients with COVID-19 may also present to the hospital with different neurological symptoms (loss of sense of smell or taste, headache, muscle pain, impaired consciousness, dizziness, stroke and seizures) [10]. In addition, the presence of, dizziness, vomiting, nausea, myalgia, hyposmia, and altered consciousness in patients infected with COVID-19 may also indicate neurological involvement [11].

In this study, we analyzed patients who were diagnosed with stroke in our emergency department (ED) during the pre-pandemic and pandemic times. We recorded the patients' age, sex, laboratory findings, arterial blood pressure, clinical features, radiological imaging methods, medical history, acute treatment methods, length of stay in the hospital [service or intensive care unit (ICU)] and mortality rates. Our aim was to examine the effects of the COVID-19 pandemic on stroke by comparing the clinical presentation, radiological imaging findings and treatment results of patients during both times.

Materials and Methods

Case Selection and Data Collection

Ethics committee approval was obtained for the study from Malatya Clinical Research Ethics Committee (date: 23.12.2020, decision number: 2020/199). The study included patients that presented to the ED with a stroke over the same four-month time in 2019 (pre-pandemic) and 2020 (pandemic). Patients with metabolic and infectious conditions likely to be confused with stroke, subarachnoid hemorrhage, vascular aneurysm, subdural-epidural hemorrhage, or arteriovenous malformation, those with a positive result in the polymerase chain reaction test for COVID-19, and those with COVID-19 pneumonia were excluded from the study. The information of stroke cases were retrospectively screened from the hospital automation system. The patients' age, sex, blood pressure, clinical features, laboratory findings, radiological imaging methods used [computerized tomography (CT), magnetic resonance imaging, color flow doppler ultrasonography (USG), CT angiography and digital subtraction angiography], history of diseases, acute treatment methods used (intravenous thrombolytic therapy, interventional angiography, and mechanical thrombectomy), length of stay in the hospital (service or ICU) and mortality rates were recorded. Recurrent stroke status was evaluated according to the use of anticoagulant and antiaggregant agents. The acute ischemic stroke cases were grouped according to the BAMFORD classification based on the neurological examination findings observed at the time of arrival at the ED. Total anterior cerebral infarction (TACI); is a clinical picture in which hemiparesis, cortical deficit (such as aphasia, neglect) and homonymous hemianopsia findings all come together. It indicates proximal occlusion of the middle cerebral artery (MCA) or occlusion of the internal carotid artery. Partial anterior cerebral infarction (PACI); is the clinical picture in which only two of the three findings constituting TACI are present. It refers to the occlusion of one of the branches of the MCA or the anterior cerebral artery (ACA) [12]. Posterior cerebral infarction (POCI); is a clinical picture with hemianopsia, brainstem or cerebellar findings. It indicates occlusion of the arteries of the vertebrobasilar system. Lacunar infarction (LACI); is a clinical picture in which only motor or sensory findings are affected at least two or all of the face, arms and legs. Indicates occlusion of one of the penetrating arteries [12].

Statistical Analysis

Statistical analysis of all data obtained was done using IBM SPSS. Numerical data obtained through measurements were presented as mean and standard deviation, while numerical categorical data were presented as numbers (n) and percentages (%). The statistical analysis of categorical variables was undertaken with the Pearson chi-square test. Student's t-test and chi-square test were used to compare the variables between the two groups. One-way analysis of variance was used to compare four independent groups with a normal distribution. A p value of <0.05 was considered statistically significant in all tests.

Results

In the pre-pandemic time, 74 (50%) male and 74 (50%) female patients were admitted to the ED with stroke symptoms. Ischemic stroke was present in 87.8% (n=130) of these patients and hemorrhagic stroke in 12.2% (n=18). During this time, the mean age of the ischemic stroke group was 73.42±12.70 years and that of the hemorrhagic stroke group was 74.44±10.47 years. In the pandemic time, there were 112 (55.7%) male and 89 (44.3%) female patients presenting with stroke symptoms. The subtype of stroke was ischemic 88.1% (n=177) of these patients and hemorrhagic in 11.9% (n=24) (Table 1) (Figure 1). During the pandemic time, the mean age of the ischemic stroke group was 70.94±13.99 years and that of the hemorrhagic stroke group was 69.25±14.36 years. We found no statistically significant difference between both times in terms of the stroke subtype, age, and sex.

Table 1. Demographic data of stroke cases for the pre-pandemic and pandemic periods

Variables		Pre-pandemic		Pandemic	
		n	(%)	n	(%)
Sex	Male	74	50	112	55.7
	Female	74	50	89	44.3
Stroke subtype	Hemorrhagic	18	12.2	24	11.9
	Ischemic	130	87.8	177	88.1
Comorbid diseases	Hypertension	88	55.2	146	73.1
	Coronary artery disease	64	43.3	102	50.7
	Hyperlipidemia	28	18.9	23	11.4
	Diabetes mellitus	8	5.5	49	24.4
	Atrial fibrillation	80	54	105	52.2
Mortality status	Exitus	20	13.5	25	12.5
	Survived	128	86.5	176	87.5

In the pre-pandemic time, the mean systolic and diastolic arterial blood pressure values were 150.04±18.12 mmHg and 87.48±8.01 mmHg, respectively for the ischemic stroke cases and 199.83±25.72 mmHg and 109.33±31.67 mmHg, respectively for the hemorrhagic stroke group. Among the patients presenting during the pandemic time, the mean systolic and diastolic arterial blood pressure values were 161.85±18.04 mmHg and 92.07±7.85 mmHg, respectively for the ischemic stroke group and 206.16±19.31 mmHg and 117.33±13.80 mmHg, respectively for the hemorrhagic stroke cases. Mean systolic and mean diastolic arterial blood pressure values in the hemorrhagic stroke groups in both times were significantly higher ($p<0.001$ for both).

When the comorbid diseases of the patients were examined, hypertension (55.2%), coronary artery disease (43.3%), hyperlipidemia (18.9%), and diabetes mellitus (5.5%) were the most common chronic diseases in the pre-pandemic time. While

the rate of coronary artery disease was statistically significantly higher in patients who had ischemic stroke (p=0.004), the rate of hypertension was statistically significantly higher in those who had hemorrhagic stroke (p=0.009). During the pandemic time, hypertension (73.1%), coronary artery disease (50.7%), diabetes mellitus (24.4%), and hyperlipidemia (11.4%) were the most common comorbidities (Table 1). Atrial fibrillation was the most common cardiac pathology in the ischemic stroke group in both times (62.1%, n=80 for the pre-pandemic time and 59.3%, n=105 for the pandemic time). In the ischemic stroke group, similar recurrent stroke rates were observed for the pre-pandemic (10%, n=13) and pandemic (14.7%, n=26) times. When the antiaggregant and anticoagulant treatments used by the patients with recurrent ischemic stroke were examined, it was observed that the rate of recurrent stroke was significantly higher in those receiving new-generation oral anticoagulant treatment during the pre-pandemic time (p=0.043) while this rate was higher in those using acetylsalicylic acid during the pandemic time (p<0.001).

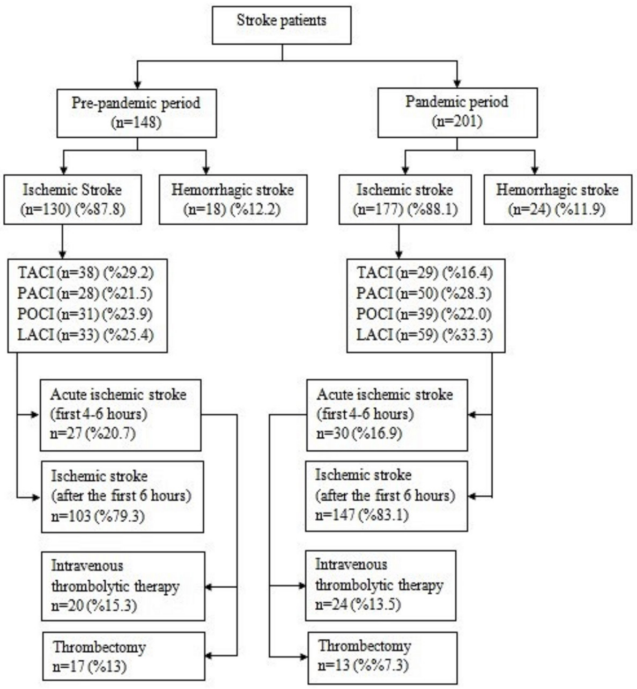

Figure 1. Pre-pandemic and pandemic period stroke patients, BAMFORD classification and treatments of ischemic stroke

According to the BAMFORD classification of ischemic stroke among patients presenting to the ED during the pre-pandemic time, TACI was observed at a rate of 29.2% (n=38), PACI at 21.5% (n=28), POCI at 23.9% (n=31), and LACI at 25.4% (n=33) (Figure 1). During the pandemic time, TACI was present in 16.4% (n=29) of the patients, PACI in 28.3% (n=50), POCI in 22% (n=39), and LACI in 33.3% (n=59) (Figure 1). Table 2 shows the ischemic stroke presentations for both times. In the pandemic time the number of patients with TACI presentations significantly decreased when compared to both time (p=0.008) (Table 2).

Intravenous thrombolytic therapy was applied to 15.3% (n=20) of the ischemic stroke cases during the pre-pandemic time, and interventional angiography and thrombectomy were applied to 13% (n=17). Patients who had ischemic stroke, intravenous thrombolytic therapy was performed in 13.5% (n=24) and interventional angiography and thrombectomy in 7.3% in the pandemic time (n=13). Of the patients with ischemic stroke who applied to the ED, those who applied within the first 4-6 hours were considered as acute ischemic stroke. During the pandemic time, the rate of acute ischemic stroke presentations was low, and the rate of patients who underwent interventional angiography and thrombectomy was also low (Table 3) (Figure 1).

Carotid and vertebral doppler USG were performed in 102 (78.4%) patients with an ischemic stroke In the pre-pandemic time, and a significant stenosis of 70% or greater was detected in 19.6% (n=20). In the pandemic time, carotid and vertebral doppler USG vascular examinations were performed in 95 (53.6%) patients, with a significant stenosis of 70% or greater being observed in 18.9% (n=18). In vascular imaging when both times are compared, the number of carotid and vertebral doppler USG examinations was found to be lower during the pandemic time (p=0.906).

When hospital stay was examined according to the presentation time, the mean length of stay in the ICU was 5.93 days and the total duration of hospitalization was 11.06 days for the pre-pandemic time, while these durations were 5.60 days and 9.25 days, respectively for the pandemic time. Although both durations were shorter for the pandemic time, there was no significant difference compared to the pre-pandemic time. Considering the mortality status of the stroke cases, 13.5% (n=20) of the patients died during the pre-pandemic time and 12.4% (n=25) during the pandemic time, indicating no significant difference (p=0.683).

Table 2. BAMFORD classification of ischemic stroke for the pre-pandemic and pandemic periods

	Pre-pandemic		Pandemic		p¶
	n	(%)	n	(%)	
TACI	38	29.2	29	16.4	*0.008
PACI	28	21.5	50	28.3	0.175
POCI	31	23.9	39	22.0	0.710
LACI	33	25.4	59	33.3	0.127
TOTAL	130	100	177	100	

TACI: Total anterior cerebral infarction PACI: Partial anterior cerebral infarction
POCI: Posterior cerebral infarction LACI: Lacunar infarction
*:Significant p value ¶Chi-square test

Table 3. Details of ischemic stroke cases and treatments applied

	Pre-pandemic		Pandemic		pµ
	n	(%)	n	(%)	
IV thrombolytic therapy	20	15.3	24	13.5	0.654
Thrombectomy	17	13	13	7.3	0.106
Acute ischemic stroke (within the first 4-6 hours)	27	20.7	30	16.9	0.400
Ischemic stroke (after the first 6 hours)	103	79.3	147	83.1	
Total ischemic stroke	130	100	177	100	

µ Chi-square test
IV: Intravenous

Discussion

Stroke is one of the most serious neurological manifestations of COVID-19 infection. The virus that causes COVID-19 infection can result in the development of stroke by affecting the vascular structure and increasing coagulation. With endothelial cells being damaged, inflammatory and thrombotic pathways are activated, and consequently coagulopathy develops [10]. Studies investigating the pathophysiology of ischemic stroke during the pandemic have mainly focused on three main topics: hypercoagulability, vasculitis, and cardiomyopathy [13,14]. The incidence of stroke due to COVID-19 infection is generally reported to be 5-6%. Cerebrovascular symptoms begin on average 10 days after respiratory complaints [15].

At the beginning of the pandemic, a study reported that neurological complications were seen in 36% of 214 patients followed up due to COVID-19. Among these patients, stroke was detected in 2.8% (n=6), of whom only one had a hemorrhagic stroke while the remaining five had an ischemic stroke [9]. This is similar to the distribution reported for stroke subtypes [16]. In another study found that the risk of ischemic stroke increased by 5% during COVID-19 infection (95% confidence interval: 2.8-8.7%). The incidence of hemorrhagic stroke during COVID-19 infection was found to be very low compared to ischemic strokes [17]. In our study, there was an increase in the number of patients presenting with both ischemic and hemorrhagic stroke during the pandemic time.

The high prevalence of hypertension in the general population continues to be the most important modifiable risk factor in both ischemic and hemorrhagic stroke cases [18]. It has been observed that the incidence of stroke can be reduced by 35-44% through effective blood pressure regulation [19]. The most common cardiac risk factor is atrial fibrillation in the etiology of ischemic stroke [20]. Similar to the literature, we found that atrial fibrillation was the most common cardiac risk factor in the etiology of ischemic stroke during both times. In addition, when the comorbid diseases of the patients were examined, hypertension was the most common in both times.

In a study evaluating pre-pandemic and pandemic times, it was reported that there was a decrease in the frequency of patient presentations with stroke during the pandemic time without any significant difference in the severity and early-term outcomes related to this condition [21]. In a multicenter study conducted in Germany, stroke cases in the first 15-week time in 2019 and 2020 were compared, and a decrease in the incidence of acute ischemic stroke cases was observed, especially in 2020. The authors mostly attributed this to the patients' feeling that they had to avoid entering possible infection environments [22]. Similarly, in our study, we observed a decrease in the rate of patients presenting with acute ischemic stroke and detected a decrease in patient presentations in the acute time of stroke.

Number of ischemic strokes Altunisik and Arik observed a 44% decrease, 62.5% in the number of intracranial hemorrhages, and 87.5% in the number of transient ischemic attacks among hospital admissions evaluated during the pandemic time [23]. It is note worthy that in our study, there was an increase in stroke cases presenting to our hospital during this time. We consider that this may be related to our hospital being a well-equipped stroke center in this region and patients' growing awareness of stroke indications despite the pandemic conditions. However, as seen in our study, when the two times were compared, the total length of hospital stay of the patients was significantly shorter during the pandemic time. This may also be related to the intensified fear of contracting the virus experienced by patients and their relatives due to the pandemic.

In a study conducted, the effect of the 'stay-at-home' order on hospital presentation times, stroke subtypes, and treatment methods were examined, and it was shown that a significant increase was in the time from 'last known well' to emergency presentation during the pandemic [24]. In the same study, a significantly higher number of patients were reported to undergo mechanical thrombectomy due to large vessel occlusion during the pandemic time, which was considered to be related to the cytokine storm caused by COVID-19 [24]. In our study, although the total number of ischemic stroke cases increased during the pandemic time, we observed in the number of those presenting with an acute ischemic stroke a decreasing. Delays in presentation to the ED resulted in the number of patients decreasing that could be treated with intravenous thrombolytic therapy, angiography, and mechanical thrombectomy.

Scoring systems developed for stroke facilitate the prediction of the severity of neurological sequelae, determination of the location of vascular occlusion, and prediction of early prognosis [25]. Another important classification of ischemic stroke cases adopted in clinical practice is the BAMFORD classification [12]. This simple and easily applicable classification is based on basic neurological findings without taking into account etiological features. Among the components of this classification system,TACI refers to the co-existence of acute hemiparesis or hemiplegia, highcortical disorder, and homonymhemianopsia; PACI refers to the presence of two of the three neurological findings seen in TACI; LACI refers tothe motor and/or sensory involvement of all three or two areas of the face, arm and leg without cortical signs and hemianopsia; and POCI refers to the presence of findings due to the proximal or distal occlusion of the brain stem (e.g., bilateral motor and/or sensory deficits, cranial nerve findings, and gaze limitations) or the presence of any or all cerebellar findings and isolated hemianopsia [12,26,27]. In our study, the BAMFORD classification of ischemic stroke cases were performed in order to predict the clinical course of the patients, and a significant decrease was observed in the number of those diagnosed with TACI during the pandemic time. This suggests that anterior system infarction may be seen less frequently during the pandemic time when compared both times.

In some studies examining the collateral damage caused by the COVID-19 pandemic, patients with many serious health problems, such as cancer surgery and heart attack during the pandemic time avoid visiting the hospital due to the fear of contracting the virus or stay-at-home orders, which may lead to an increase in long-term morbidity and mortality rates [28,29]. We determined that sroke was one of these health problems. Although we did not see a significant difference in early mortality rates in our study, we attributed the decreased number of acute ischemic stroke presentations to the pandemic conditions. In addition, we considered that the decrease in the number of patients receiving acute treatment for stroke due

to delayed presentation to the hospital during the pandemic would have negative effects on the long-term disability and morbidity of these patients.

Limitations of Study

Although this study is one of the few studies examining stroke cases from the pre-pandemic and pandemic perspective, its power to represent the overall patient population is limited due to the short duration of the study and the small number of patients. In addition, the patients' modified Rankin scale scores at both follow-up and discharge were unknown in both times, which limits the predictability of long-term outcomes.

Conclusion

Although the number of stroke cases increased during the pandemic time, the rate of presentations with acute ischemic stroke decreased. This decrease in early admissions caused patients to lose their chance for acute medical and interventional treatment. These delays, which may be related to the patients' fear of contracting the virus, may result in the worsening of disability rates in the long term. Therefore, properly informing patients concerning this situation will reduce collateral damage due to stroke.

Conflict of interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
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Ethical approval
The study was approved by Malatya Clinical Research Ethics Committee with the 2020/199 decision number, dated 23.12.2020.

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