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Ischemic Stroke During the Pandemic in a Secondary Care Hospital: COVID-19 and Its Collateral Effects

İkinci Basamak Bir Hastanede Pandemi Döneminde İskemik İnme: COVID-19 ve Kollateral Etkileri

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ABSTRACT

Aim: Ischemic stroke is among the leading causes of death and disability. Although recent studies have shown a possible relationship between COVID-19 and ischemic stroke, the effect of the pandemic period, which may be another factor in the increase of ischemic stroke risk factors, has not been investigated. Therefore, in current study, we assessed how the COVID-19 pandemic affected ischemic strokes.

Material and Methods: Patients were divided as two years before and after the first COVID-19 case in Turkey, and their COVID-19 history, demographic characteristics and clinical features (comorbid diseases, etc.) were obtained.

Results: There were 588 ischemic stroke patients pre-pandemic and 694 ischemic stroke patients post-pandemic. In post-pandemic periods, 322 patients were vaccinated, and 288 patients were not. No significant difference in ischemic stroke was found between vaccinated and unvaccinated groups ($p = 0.168$) and between different vaccine-type groups ($p = 0.873$). Partial anterior circulation infarct (PACI) was the most common ischemic stroke subtype in both groups; there was no difference between them ($p=0.719$). The number of ischemic stroke were significantly increased in the post-pandemic period ($p<0.001$). Although patients in the post-pandemic period were younger ($p<0.001$), they had more comorbid diseases (diabetes mellitus, hypertension, hyperlipidemia, cardiovascular diseases) for ischemic stroke (p respectively; <0.001, <0.001, 0.032, 0.005). Also, eleven patients (1.6%) had concurrent acute ischemic stroke and COVID-19, and just three (0.4%) had a COVID-19 history.

Conclusion: Current study showed an increased number of patients with acute ischemic stroke after the pandemic. This finding, while preliminary, suggests that the pandemic period may be an independent risk factor for ischemic stroke.

Keywords: COVID-19, ischemic stroke, pandemic

ÖZ

Amaç: İskemik inme, dünya genelinde mortalite ve morbiditeye neden olan en yaygın nedenlerden biridir. Her ne kadar son çalışmalar ile COVID-19 ve iskemik inme arasındaki ilişki gösterilmiş olsa da iskemik inme prevelansını arttırabilecek diğer bir faktör olan pandemi dönemi üzerinde yeterli sayıda çalışma yapılmamıştır. Bu yüzden, bu çalışmada COVID-19 pandemi döneminin iskemik inme üzerindeki etkisinin araştırılması amaçlanmıştır.

Gereç ve Yöntemler: Mart 2018 ve Mart 2022 dönemleri arasında iskemik inme tanısı almış olan hastalar retrospektif olarak tarandı. Hastaların COVID-19 öyküsü, demografik ve klinik özellikleri (iskemik inme için eşlik eden komorbid faktörler vs.) Türkiye'deki ilk COVID-19 vakasından 2 yıl önce ve sonraki dönem olmak üzere iki gruba ayrılarak karşılaştırıldı.

Bulgular: Çalışmaya pandemi öncesi 588, pandemi sonrası dönemde ise 694 iskemik inme hastası dahil edildi. Pandemi sonrası dönemdeki hastaların 322'si aşılı iken, 288'i aşısız idi. Aşılı ve aşısız gruplar arasında (p=0.168) ve farklı aşı tipi grupları arasında (p=0.873) iskemik inme açısından anlamlı fark saptanmadı. Parsiyel ön dolaşım infarktı iki grupta da en sık görülen iskemik inme alt tipiydi ve gruplar arasında fark saptanmadı (p=0.719). Pandemi sonrası dönemde iskemik inme geçiren hastaların oranı anlamlı derecede yüksekti (p<0.001). Pandemi sonrası dönemdeki hastalar daha genç olmasına rağmen (p<0.001), iskemik inme için risk faktörü olan hastalıkların (diyabet, hipertansiyon, hiperlipidemi, kardiyovasküler hastalık) daha fazla eşlik ettiği görüldü (sırasıyla p; <0.001, <0.001, 0.032, 0.005). Ayrıca 11 hastada (%1,6) akut iskemik inme ve COVID-19 birlikte görülürken, sadece üç hastanın (%0,4) inme öncesi COVID-19 öyküsü vardı.

Sonuç: Çalışmamız iskemik inme sayısında pandemi sonrası anlamlı bir artış olduğunu ve yaş ortalamasının çok daha düşük olmasına rağmen eşlik eden risk faktörlerin daha fazla olduğunu göstermiştir. Pandemi döneminin iskemik inme için COVID-19'dan bağımsız bir risk faktörü olabileceğini gösteren bu bulgular daha fazla hasta sayılı çalışmalar ile desteklenmelidir.

Anahtar Sözcükler: COVID-19, iskemik inme, pandemi

INTRODUCTION

Globally, stroke is one of the leading causes of death and disability, and 87% of strokes are ischemic (1,2). Despite new treatments being constantly improved, mortality and morbidity remain major problems. The most known etiologies are age, sex, diabetes mellitus (DM), hyperlipidemia (HL), cardiovascular diseases (CVD), diet, sedentary life, hypertension (HT), and hypercoagulability syndromes (3). Also, acute ischemic stroke (AIS) has recently appeared as both a presenting feature and complication of Coronavirus disease 2019 (COVID-19) (4-6).

COVID-19 is an severe infectious disease caused by the SARS-CoV-2, and it was declared as a pandemic on March 11, 2020 (7, 8). Its characteristic features are usually pneumonia, cough, fever, and fatigue (9,10). However, COVID-19 has been reported to affect almost every organ system with a broad range of symptoms and severity (11). It has been shown that one-third of COVID-19 patients may have neurological symptoms such as loss of smell and taste or, more seriously, AIS (4). Coagulopathy caused by antiphospholipid antibodies or endotheliopathy has been implied to be responsible for the underlying pathophysiology of the AIS mechanism in COVID-19 patients (12-14).

To date, many studies have investigated whether SARS-CoV-2 itself is the etiology of ischemic stroke (15–17). However, considering the pandemic period, increased sedentary life due to quarantine and accordingly increased many comorbidities such as DM, HT, HL, obesity, etc., may have caused AIS too. We aimed to investigate how the COVID-19 pandemic affected ischemic strokes. Our main hypothesis is that lifestyle change due to the pandemic period is another critical etiological factor for ischemic stroke.

MATERIAL and METHODS

We conducted a retrospective study with patients who applied to our hospital between March 1, 2018, and March 1, 2022, and were diagnosed with acute ischemic stroke. The diagnosis was made by a neurologist clinically and radiologically. March 11, 2020 marked the first report of COVID-19 in Turkey. Therefore, patients were divided as two years before and after this date, to investigate the COVID-19 pandemic's effect on ischemic stroke. Demographic characteristics (age, gender) and clinical variables (comorbid diseases) were obtained from the two groups. In conjunction with this study, Antalya Education and Training Hospital Ethics Committee approved the protocol (date: 18.08.2022, decision number: 12/20). Helsinki Declaration principles were followed in this study.

Inclusion Criteria: Adult patients (older than 18 years old) who have a certain diagnosis of acute ischemic stroke (clinically and radiologically confirmed) between March 1, 2018, and March 1, 2022. Exclusion Criteria: Patients presenting primarily with hemorrhage, tumor, and vasculitis. Patients with no clinical data.

Statistical Analysis

The statistical analysis was conducted using SPSS version 28.0 (SPSS Inc., Chicago, Illinois, USA). For continuous variables, the mean and standard deviation, and for categorical variables, the frequency and percentage were computed as descriptive variables. As a measure of normality, histograms and Shapiro-Wilk tests were used. For comparisons; based on the normality distribution, for continuous variables; unpaired t-test, and for categorical variables; chi-squared test of independence were used. As a significant value, p<0.05 was accepted.

RESULTS

A total of 2136 patients were retrieved from the hospital database, from which 854 patients were removed because of hemorrhagic stroke or subdural/epidural hematoma. Finally, we included 1282 patients diagnosed with ischemic stroke in the study. The mean age of the patients was 69.97±13.6 years, and 457 (35.6%) were female. This study examined 588 patients who had ischemic strokes prior to the pandemic. Patient age ranged from 72.7 to 13.3 years; 34.7% were females. In the post-pandemic period, 694 patients with ischemic stroke were included in the study. The mean

age of patients was 67.6±13.4 years, and 253 (36.4%) were female. Of those, three patients had a history of COVID-19, and eleven patients were hospitalized with concurrent acute ischemic stroke and COVID-19. Among these patients, 322 were vaccinated, and 288 were not vaccinated (Table 1). The groups did not differ significantly (p=0.168) and the vaccine type groups did not differ too (p=0.873). Partial anterior circulation infarct (PACI) was the most common ischemic stroke subtype in both groups; there was no difference between them. Also, we quantified the stroke severity in two groups by NIHSS (National Institutes of Health Stroke Scale Scores). The scale includes 11 categories that evaluate specific abilities (awareness, eye movement, visual field, facial palsy, arm and leg motor function, cerebellar function, sensory function, language and speech skills, and presence of neglect). It has a range of 0 to 42 points, which allows us to categorize stroke severity as mild (<5 points), moderate (5 to 15 points), moderate to severe stroke (16 to 20 points), and severe stroke (21 to 42 points) (18). The majority of patients in both groups had moderate stroke severity (5-15) according to NIHSS and frequency was similar in both groups (Table 1). A comparison of the two periods reveals a significant increase in cases of ischemic stroke after the pandemic (p <0.001). Another important finding was that patients were significantly younger after the pandemic than before (p<0.001). Most of the patients were male in both periods, and No statistically significant difference was observed between the groups (p=0.5). When we investigated the comorbidities, we found that the number of patients with DM, HT, HL, and CVD in the post-pandemic period was significantly higher (Figure 1). Further demographic and clinical data were provided in Table 1.

Table 1: Demographic and clinical characteristics of patients

Demographic and clinical characteristics	Between 2018-2020 (n=588)	Between 2020-2022 (n=694)	p
Age (year ±SD)	72.7±13.3	67.6±13.4	<0.001
Gender (F*)	204 (34.7)	253 (36.4)	0.514
DM, n (%)	47 (7.9)	87 (14.8)	<0.001
HT, n (%)	95 (16.2)	225 (32.4)	<0.001
HL, n (%)	41 (7)	72 (10.4)	0.032
CVD, n (%)	20 (3.4)	51 (7.3)	0.005
COVID-19		3 (0.4)** 11 (1.6)***	
Types of Vaccine, n (%)			0.873
1 dose of Sinovac		59 (8.5)	
2 doses of Sinovac		65 (9.4)	
3 doses of Sinovac		67 (9.6)	
3 doses of Sinovac + 1 dose of Biontech		70 (10.1)	
3 doses of Sinovac + 2 doses of Biontech		61 (8.8)	
None		288 (41.5)	0.168
Unknown		84 (12.1)	
Subtypes of Stroke, n (%)			
TACI	104 (18)	106 (15)	0.148
PACI	260 (44)	296 (43)	0.719
LACI	141 (24)	174 (25)	0.678
POCI	83 (14)	118 (17)	0.140
NIHSS, n (%)			
1-4	71 (12)	104 (15)	0.140
5-15	370 (63)	416 (60)	0.118
16-20	100 (17)	125 (18)	0.271
21-42	47 (8)	49 (7)	0.497

F:** female, ** (history of COVID-19), (concurrent with AIS) **DM:** diabetes mellitus, **HT:** hypertension, **HL:** hyperlipidemia, **CVD:** cardiovascular diseases, **AIS:** acute ischemic stroke, **TACI:** total anterior circulation infarcts, **PACI:** partial anterior circulation infarcts, **LACI:** lacunar infarcts, **POCI:** posterior circulation infarcts, **NIHSS;** National Institutes of Health Stroke Scale Scores

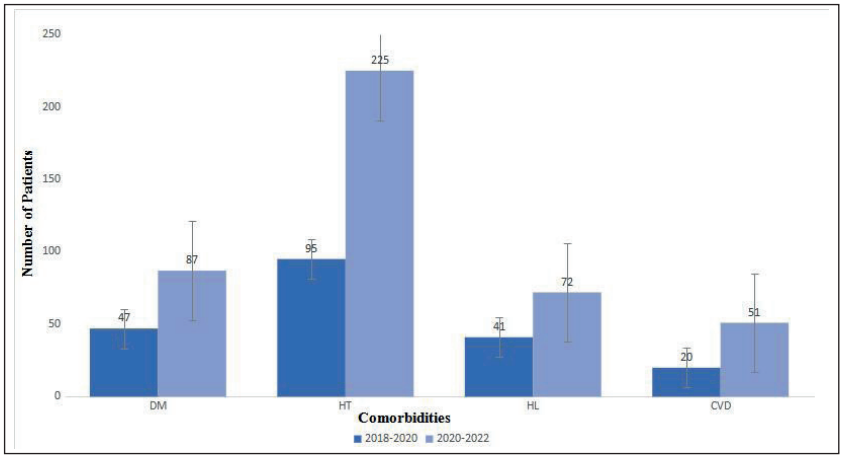

Figure 1: Comorbidity levels based on years.
DM: diabetes mellitus, **HT:** hypertension, **HL:** hyperlipidemia, **CVD:** cardiovascular diseases

DISCUSSION

Our results provided several valuable insights: 1) In the post-pandemic period, the number of patients with AIS has increased significantly; 2) patients with AIS in the post-pandemic period were younger than in the pre-pandemic period; 3) comorbidities accompanying AIS are more common in the post-pandemic period than in the pre-pandemic period.

When all these results are put together, increased sedentary behavior during quarantine and the consequent increase in comorbidities can be considered as the source of the increase in AIS. This idea seems reasonable considering another result of the current study: increased DM, HT, HL, and CVD in the post-pandemic period. In accordance with the present results, previous studies have demonstrated a clear relationship between AIS and a sedentary lifestyle (19,20). Researchers believe excessive sedentary behavior leads to muscle loss, which may contribute to cardiovascular disease and stroke (21,22). Also, an observational study with 15,364 participants found that those whose sedentary time was >8 hours per day had a high risk of stroke (23). Moreover, decreased physical activity can lead to insulin resistance, obesity, and, finally, metabolic syndrome, which is another risk factor for AIS (24,25). Another recent study revealed that BMI increased, and insulin resistance and lipid parameters worsened in obese patients during the COVID-19 quarantine period, regardless of diet and exercise (26); additionally, it is essential to highlight that the post-pandemic period patients were younger than the pre pandemic period, and these younger patients had more AIS comorbidities. AIS comorbidities are typically known to be positively associated with age, but this is inconsistent with our results. Therefore, these comorbidities are likely to have another underlying cause. Thus, this result further supports the idea that sedentary lifestyle changes may cause such comorbidities and, ultimately, AIS. Since all these diseases are linked to each other, it is not surprising to find increased these comorbidities during the pandemic period and, finally, an increased number of AIS.

Also, it has been reported that SARS-CoV-2 itself can be an independent risk factor for AIS. Several reports have shown a strong relationship between morbidity/mortality and HT, DM, and CVD in patients diagnosed with COVID-19 (27-31). Although we found only eleven patients with concurrent COVID-19 and AIS, and three patients had a history of COVID-19, we do not know the prevalence of stroke patients with asymptomatic or minimally symptomatic COVID-19 infection who were not admitted to the hospital. And it is obscure whether those patients are similarly at risk for AIS as patients with apparent infection (32). Therefore, although we could not confirm the positivity of COVID-19 in asymptomatic patients, there is a possibility that asymptomatic or mildly symptomatic cases of COVID-19 may contribute to the increase in AIS.

There was no significant difference in gender between the periods, and it is not surprising that most patients in both groups were male, considering male is a recognized risk factor for AIS. Our finding contradicts the previous study, which suggested that the number of AIS patients decreased during the pandemic (33). This contradictory finding could be due to the time frame taken into account. They have investigated the two months period after the onset of the pandemic, which may not be sufficient to observe the long-term impact of the COVID-19 infection and the pandemic period.

Another finding was that although there was a trend toward the vaccinated group having ischemic stroke, no significant difference was observed. However, since vaccination began after a certain time of quarantine period, this trend needs to be interpreted carefully. Because vaccinated patients had already been quarantined for a longer time, they were exposed to a sedentary life for longer. Therefore, we cannot directly conclude whether the increase in ischemic stroke is due to the vaccine or the quarantine period. We also did not

find any difference between different vaccine type groups. However, since the results are limited to a certain period, studies with longer follow-ups are needed to see the long-term effects of vaccines on patients.

Our study had several limitations – first, we couldn't include the asymptomatic or mildly symptomatic cases of COVID-19. Second, we didn't have the patient's BMI information to show the obesity risk. Finally, since it is a retrospective study, it can determine the association rather than causation.

CONCLUSION

The aim of the present research was to investigate SARS-CoV-2 and its collateral impact on AIS. This study showed that COVID-19 increased AIS during the pandemic period. A contribution of this study was to confirm that COVID-19 may also be a risk factor for AIS through its collateral effects, besides being an independent risk factor. These findings provide valuable insights into behavior during possible future outbreaks. Further research with a larger sample size that includes contact tracing or surveillance programs for risk-stratified populations would be a useful way to resolve the discrepancy of the asymptomatic COVID-19 effect on AIS.

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Author Contributions

Concept, Design, Analysis, and Interpretation: **Elif Uygur Kucukseymen,** Data Processing: **Senay Ozturk, Ebru Balaban,** Writing: **Senay Ozturk, Ebru Balaban.**

Conflicts of Interest

There is no conflict of interest.

Financial Support

There was no funding for this research.

Ethical Approval

The study was conducted with the permission of the XXX Ethics Committee (Date: 18.08.2022, Decision No: 12/20). All procedures were performed in compliance with the Declaration of Helsinki.

Review Process

Extremely peer reviewed and accepted

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