TURKISH JOURNAL OF INTERNAL MEDICINE

ISSN:2687-4245

Neurology

Clinical comparison of acute stroke cases with and without COVID-19

Hatice Barut[1], **Cemile Haki**[1], **Mustafa Barut**[2]

[1]Department of Neurology, Bursa City Hospital, Bursa, Turkey
[2]Department of Internal Medicine, Bursa City Hospital, Bursa, Turkey

ABSTRACT

Background We aimed to assess acute stroke cases with and without coronavirus disease 2019 (COVID-19) positivity concerning clinical features and the number of hospitalizations acute stroke cases compared to the previous year.

Methods Acute stroke patients with and without COVID-19 positivity, including those who were hospitalized in the neurology service and intensive care unit of tertiary healthcare center between 17 December 2020 and 31 January 2021 due to acute stroke, were included in this cross-sectional study.

Results Mortality (p=0.042) and mechanical ventilation use (p=0.041) were more frequent in COVID-19-positive stroke patients compared to those without COVID-19. The most common type of stroke in COVID-19-positive acute stroke patients was ischemic stroke (69.23%). Additionally, stroke patients with COVID-19 had a significantly higher percentage of kidney disease compared to those without COVID-19 (p=0.009). We also observed that the number of acute stroke cases hospitalized in our hospital during the pandemic decreased significantly compared to the previous year (p=0.036).

Conclusion Since the majority of our patients were diagnosed with COVID-19 after admission to the hospital due to stroke, it should be kept in mind that patients who apply to the hospital with stroke symptoms may also have COVID-19, even if they are asymptomatic.

Turk J Int Med 2024;6(2):81-89
DOI: 10.46310/tjim.1293458
Original Article

Keywords: *COVID-19, acute cerebrovascular disease, stroke, symptoms*

Received: *May 10, 2023;* ***Accepted:*** *January 30, 2024;* ***Published Online:*** *April 29, 2024*

How to cite this article: *Barut H, Haki C, Barut M. Clinical comparison of acute stroke cases with and without COVID-19 Turk J Int Med 2024;6(2):81-89. DOI: 10.46310/tjim.1293458*

Address for Correspondence:
Hatice Barut, MD.,Department of Neurology, Bursa City Hospital, Doğankoy 16110 Nilufer/Bursa, Turkey

E-mail: drhbarut@gmail.com

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has affected the whole world in a very short time and still continues to exist as a public health threat. While severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is known to cause interstitial pneumonia and acute respiratory distress syndrome, there is increasing evidence that it causes encephalopathy[1], limbic and brainstem encephalitis[2,3], Guillain-Barré syndrome[4,5], and stroke (predominantly ischemic stroke, but also hemorrhagic stroke).[6-10]

Stroke is a serious cause of morbidity and mortality, and data concerning its incidence during the pandemic period, its association with COVID-19 infection, and its course in infected individuals are increasing.[11-13] Acute cerebrovascular disease, especially ischemic stroke, may occur with SARS-CoV-2.[14-17] This study aimed to investigate acute stroke cases with and without COVID-19 positivity about the clinical features of the disease and to identify the number of hospitalisations due to acute stroke during the COVID-19 era relative to the previous year.

MATERIAL AND METHODS

According to 2022 data, the population of our city is 3,194,720. Our hospital was one of the three tertiary hospitals in our city. Additionally, there was a stroke centre in our hospital. During the pandemic between December 17, 2020 and January 31, 2021, all acute stroke patients with and without COVID-19 diagnosis were included in the study. Patients who presented to the emergency department within the first 24 hours after the onset of stroke symptoms and were diagnosed with a definitive diagnosis of stroke based on medical history, neurological examination and neuroimaging findings (brain computed tomography [CT], magnetic resonance imaging [MRI]) and hospitalised, or who underwent neuroimaging within the first 24 hours of neurological symptoms while being followed up in the hospital due to COVID-19 and were diagnosed with a definitive diagnosis of acute stroke during consultation, were included in the study.

Demographic information (age, sex, date of application), comorbid diseases (history of hypertension, diabetes mellitus, cardiovascular disease, chronic obstructive pulmonary disease [COPD], malignancy, chronic renal disease or cerebrovascular accidents), laboratory parameters at hospital admission (haemoglobin, platelet, white blood cell counts, blood glucose, urea, creatinine, erythrocyte sedimentation rate [ESR], C-reactive protein, D-dimer levels, International Normalized Ratio [INR], aPTT, and ferritin), and discharge information were prospectively recorded. Acute stroke patients with and without COVID-19 were compared in terms of demographic characteristics and laboratory results.

In addition, the number of acute stroke patients followed up in our hospital in the pandemic period (December 17, 2020, and January 31, 2021) during which the study was conducted was compared with the one-year pre-pandemic period (December 17, 2019, and January 31, 2020).

This study was approved by the local Clinical Research Ethics Committee. All protocols were conducted in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from all patients or their first-degree relatives, and only cases with informed consent were included in the study.

Statistical analysis

All analyses were performed on SPSS v21 (IBM, Armonk, NY, USA) and were evaluated for a <0.05 significance threshold for a p-value. Shapiro-Wilk test was used to check the normality of continuous variables. Continuous variables were given as mean±standard deviation in the presence of normal distribution and as median (1st-3rd quartile) in the presence of non-normal distribution. Categorical data were presented with frequency (percentage) values. Normally distributed variables were analysed with the independent samples t-test. Non-normally distributed variables were analysed with the Mann-Whitney U test. Categorical variable distributions were compared with chi-square tests or Fisher's exact test. The number of stroke cases before and after the COVID-19 pandemic was compared with the one-sample chi-square test under the null hypothesis of equal probabilities.

Table 1. Characteristics of patients with COVID-19

COVID-19 diagnosis	
PCR and CT positive	14 (53.85%)
PCR negative, CT positive	11 (42.31%)
PCR positive	1 (3.85%)
Reason for hospital application	
Other reasons	6 (23.08%)
Stroke	20 (76.92%)

Data were given as frequency (column percentage).

RESULTS

We included 64 patients (30 males and 34 females) with acute stroke in our study; the mean age was 70.14±14.46 (range 22 - 98) years. Twenty-six (40.63%) patients were COVID-19 positive. Fourteen (53.85%) patients were both polymerase chain reaction (PCR) test and thorax CT positive, 11 (42.31%) patients were PCR negative and thorax CT positive, and one (3.85%) patient was PCR positive only. Twenty (76.92%) COVID-19-positive patients had applied to the hospital because of a stroke. Six (23.08%) COVID-19-positive patients suffered from an in-hospital stroke, and the median stroke onset of these patients was 6 (range 1-16) days after hospitalisation *(Table 1)*.

There were no significant differences between patients with COVID-19 negativity and positivity concerning age and sex. Renal disease percentage was significantly higher in the positive group than in the negative group (p=0.009). There were no significant differences between groups regarding other risk factors *(Table 2)*.

The most common type of acute stroke was ischemic stroke in both groups. There were two (5.26%) transient ischemic attack cases in the COVID-19-negative group, whereas the COVID-19-positive group had one (3.85%) venous sinus thrombosis case and one (3.85%) ischemic plus hemorrhagic case. There was no significant difference between types of stroke in groups (p=0.335). Dysarthria frequency was significantly higher in the positive group than in the negative group (p=0.003). There were no significant differences between hemiparesis (p=1.000), hemi-hypoesthesia (p=0.445), hemianopsia (p=0.525), aphasia (p=0.305), and impaired consciousness (p=0.430) of both groups *(Table 2)*.

The groups were similar regarding Glasgow Coma Scale scores, thrombolytic/thrombectomy use (p=0.680), and need for intensive care unit stay (p=0.503). Ten (38.46%) patients were intubated in the positive group, while five (13.16%) patients were intubated in the negative group (p=0.041). Nine

Table 2. Summary of patient characteristics with regard to presence of COVID-19

Variables	COVID-19		Total (n: 64)	*P*-value
	Negative (n: 38)	Positive (n: 26)		
Age	72.5 (60-80)	73 (65-81)	72.5 (62-80.5)	0.477
Sex				1.000
Male	18 (47.37%)	12 (46.15%)	30 (46.88%)	
Female	20 (52.63%)	14 (53.85%)	34 (53.13%)	
Co-morbidities				
Hypertension	24 (63.16%)	16 (61.54%)	40 (62.50%)	1.000
Heart disease	20 (52.63%)	17 (65.38%)	37 (57.81%)	0.449
Diabetes mellitus	8 (21.05%)	10 (38.46%)	18 (28.13%)	0.216
COPD	8 (21.05%)	2 (7.69%)	10 (15.63%)	0.181
Malignancy	2 (5.26%)	1 (3.85%)	3 (4.69%)	1.000
Renal disease	0 (0.00%)	5 (19.23%)	5 (7.81%)	0.009
Cerebrovascular incident history	8 (21.05%)	11 (42.31%)	19 (29.69%)	0.121
Alcohol use	1 (2.63%)	0 (0.00%)	1 (1.56%)	1.000
Smoking	5 (13.16%)	3 (11.54%)	8 (12.50%)	1.000
Type of stroke				0.335
Ischemic	29 (76.32%)	18 (69.23%)	47 (73.44%)	
Haemorrhagic	7 (18.42%)	6 (23.08%)	13 (20.31%)	
Transient ischemic attack	2 (5.26%)	0 (0.00%)	2 (3.13%)	
Venous sinus thrombosis	0 (0.00%)	1 (3.85%)	1 (1.56%)	
Ischemic + haemorrhagic	0 (0.00%)	1 (3.85%)	1 (1.56%)	
Location				1.000
Anterior system	25 (86.21%)	16 (88.89%)	41 (87.23%)	
Posterior system	4 (13.79%)	2 (11.11%)	6 (12.77%)	
Stroke presentations				
Hemiparesis	28 (73.68%)	19 (73.08%)	47 (73.44%)	1.000
Hemi-hypoesthesia	17 (44.74%)	15 (57.69%)	32 (50.00%)	0.445
Hemianopsia	6 (15.79%)	6 (23.08%)	12 (18.75%)	0.525
Aphasia	13 (34.21%)	5 (19.23%)	18 (28.13%)	0.305
Dysarthria	8 (21.05%)	16 (61.54%)	24 (37.50%)	0.003
Impaired consciousness	14 (36.84%)	13 (50.00%)	27 (42.19%)	0.430
Glasgow coma scale score	14.5 (12-15)	13 (12-15)	14 (12-15)	0.229
Thrombolytic/thrombectomy	3 (7.89%)	3 (11.54%)	6 (9.38%)	0.680
Need for intensive care unit stay	16 (42.11%)	14 (53.85%)	30 (46.88%)	0.503
Intubation	5 (13.16%)	10 (38.46%)	15 (23.44%)	0.041
Mortality	4 (10.53%)	9 (34.62%)	13 (20.31%)	0.042

COPD: chronic obstructive pulmonary disease.

Data were given as mean±standard deviation or median (1st-3rd quartile) for continuous variables according to the normality of distribution and as frequency (column percentage) for categorical variables

Table 3. Laboratory measurements with regard to the presence of COVID-19

Variables	COVID-19		Total (n: 64)	*P*-value
	Negative (n: 38)	Positive (n: 26)		
White blood cell (x1000)	9.55 (7.80-12.20)	9.35 (6.84-11.70)	9.40 (7.65-12.10)	0.400
Haemoglobin	13.17±2.02	12.68±1.95	12.97±1.99	0.336
Platelet (x1000)	266.08±85.73	229.90±111.50	251.38±97.83	0.148
Lymphocyte (x1000)	1.67 (1.20-2.90)	1.21 (0.85-2.10)	1.55 (1.01-2.63)	0.042
Neutrophil (x1000)	6.55 (5.20-9.57)	6.16 (5.10-9.50)	6.30 (5.15-9.54)	0.758
Neutrophil/Lymphocyte ratio	4.00 (1.83-7.00)	4.76 (2.67-10.40)	4.18 (2.50-9.71)	0.232
C-reactive protein	4.85 (2.5-11.1)	29 (10.4-70)	9.8 (3.4-43.5)	<0.001
Ferritin	87.5 (42-183)	288 (125-824)	149 (50-288)	0.001
D-dimer	0.54 (0.31-1.2)	1.79 (0.65-6.35)	1 (0.4-2.43)	0.008
Blood glucose	123.5 (102-160.5)	155 (114-239)	131.5 (110-206)	0.086
Urea	36 (25-43)	40.5 (30-55)	37.5 (27.5-49)	0.119
Creatinine	0.88 (0.70-1.03)	0.80 (0.60-1.20)	0.86 (0.70-1.20)	0.661
AST	19.5 (16-23)	25 (18-40)	21 (17-28)	0.052
ALT	16.5 (11-20)	15 (11-25)	15.5 (11-22)	0.837
Sodium	138 (136-140)	139 (136-140)	139 (136-140)	0.762
Potassium	4.25 (3.90-4.50)	4.30 (3.90-4.60)	4.30 (3.90-4.50)	0.848

Data were given as mean±standard deviation or median (1st-3rd quartile) for continuous variables according to the normality of distribution and as frequency (column percentage) for categorical variables.

(34.62%) cases were mortal in the positive group, and four (10.53%) cases were mortal in the negative group (p=0.042) *(Table 2, Figure 1)*.

Lymphocyte count was significantly lower in the positive group than in the negative group (p=0.042). C-reactive protein (p<0.001), ferritin (p=0.001) and D-dimer (p=0.008) levels were significantly higher in the positive group than in the negative group. There were no significant differences between groups concerning other laboratory measurements *(Table 3)*.

There were 47 patients with ischemic stroke. We found no significant differences between anterior system ischemic stroke and posterior system ischemic stroke groups regarding age, sex, hemiparesis, hemi-hypoesthesia, hemianopsia, aphasia, dysarthria, and impaired consciousness *(Table 4)*.

When we evaluated the number of stroke cases before and after the COVID-19 pandemic, we found that the number of stroke cases was significantly higher in the pre-pandemic period compared to the post-pandemic period (110 vs 81, p=0.036). In addition, the number of ischemic strokes (90 vs 63, p=0.029) and cases with transient ischemic attack (13 vs 2, p=0.005) were significantly higher in the pre-pandemic compared to the post-pandemic period. There was no significant difference between the pre- and post-pandemic periods in the frequency of requiring intensive care unit stay (27 vs 30, p=0.691) *(Table 5)*.

Table 4. Summary of age, sex and symptoms of patients with ischemic stroke with regard to location

Variables	Location		Total (n: 47)	*P*-value
	Anterior system (n: 41)	Posterior system (n: 6)		
Age	73 (65 - 80)	62 (55 - 77)	72 (61 - 80)	0.285
Sex	18 (43.90%)	4 (66.67%)	22 (46.81%)	0.398
Male	23 (56.10%)	2 (33.33%)	25 (53.19%)	
Female				
Hemiparesis	28 (68.29%)	4 (66.67%)	32 (68.09%)	1.000
Hemi-hypoesthesia	20 (48.78%)	2 (33.33%)	22 (46.81%)	0.670
Hemianopsia	8 (19.51%)	0 (0.00%)	8 (17.02%)	0.571
Aphasia	14 (34.15%)	0 (0.00%)	14 (29.79%)	0.159
Dysarthria	13 (31.71%)	4 (66.67%)	17 (36.17%)	0.170
Impaired consciousness	15 (36.59%)	0 (0.00%)	15 (31.91%)	0.157

Data were given as median (1st-3rd quartile) for continuous variables according to non-normality of distribution and as frequency (column percentage) for categorical variables.

Table 5. Comparison of stroke-related data in the pre- and post-pandemic periods

Variables	COVID-19		*P*-value
	Before	After	
Number of cases	110 (57.59%)	81 (42.41%)	0.036
Type of stroke			
Ischemic	90 (58.82%)	63 (41.18%)	0.029
Haemorrhagic	7 (31.82%)	15 (68.18%)	0.088
Transient ischemic attack	13 (86.67%)	2 (13.33%)	0.005
Venous sinus thrombosis	0 (0.00%)	1 (100.00%)	N/A
Need for intensive care unit stay	27 (47.37%)	30 (52.63%)	0.691

Data were given as frequency (row percentage).

DISCUSSION

In our study, it was observed that the majority of COVID-19-positive stroke patients were admitted to the hospital due to stroke and were diagnosed with COVID-19 through subsequent examinations. The most common type of stroke in COVID-19-positive stroke patients was ischemic stroke. COVID-19-positive stroke patients had a significantly higher percentage of kidney disease and dysarthria compared to COVID-19-negative stroke patients. There was no significant difference between the groups regarding the frequency of vascular risk factors. Intravenous alteplase/thrombectomy treatment was applied to three patients with COVID-19 positivity. It was seen that mortality and mechanical ventilation used more common in COVID-19-positive stroke patients compared to stroke patients without COVID-19. In addition, we observed a significant decrease in the number of stroke cases hospitalised during the pandemic compared to the pre-pandemic period.

In patients with COVID-19, neurological symptoms may be the first reason for admission to the hospital. Also, patients admitted to the hospital with neurological symptoms without symptoms of COVID-19 may be diagnosed with COVID-19 in the tests performed.[18-22] In our study, it was observed that the majority of COVID-19-positive stroke patients were admitted to the hospital due to stroke and were diagnosed with COVID-19 through subsequent tests.

It has been reported that COVID-19-positive stroke

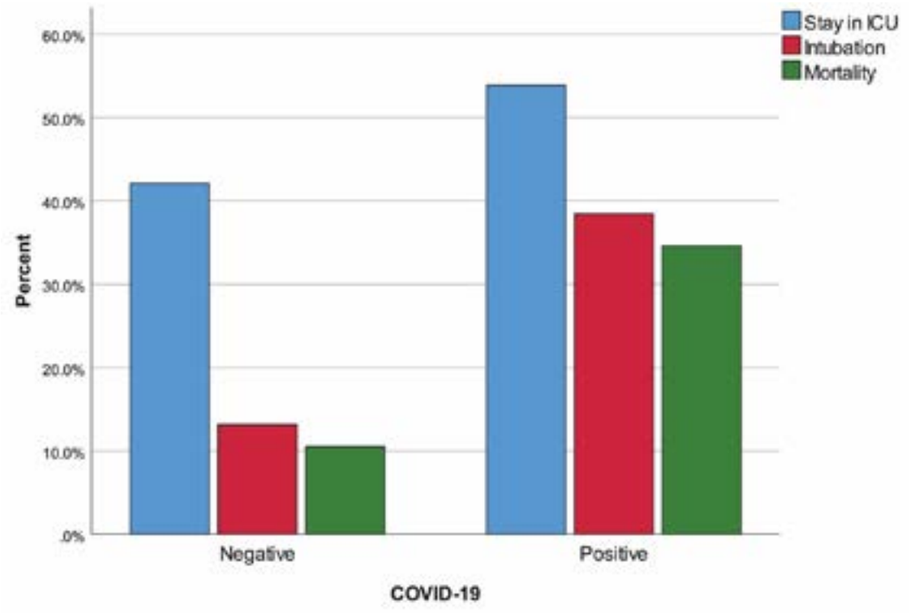

Figure 1. Intensive care unit, intubation and mortality percentages with regard to presence of COVID-19.

patients have worse outcomes, higher mortality and more frequent use of mechanical ventilation compared to stroke patients without COVID-19.[23-24] In our study, it was seen that mortality and mechanical ventilation use were more frequent in COVID-19-positive stroke patients compared to COVID-19-negative stroke patients. The high mortality rate in COVID-19-positive stroke patients is consistent with the high mortality rate in COVID-19-positive stroke patients previously reported in the literature.[25,26]

In addition, studies have emphasised that ischemic stroke is observed more frequently in COVID-19-positive stroke patients than other stroke subtypes.[18,25] In our study, we observed ischemic stroke in the majority of COVID-19-positive stroke patients. Infections, especially upper respiratory tract diseases, are a risk factor for stroke. The spike protein surface unit of SARS-CoV-2 binds with high affinity to the human ACE-2 receptor, which disrupts ANG II by affecting the normal physiological function of ACE-2, thereby causing neuronal damage and endothelial cell apoptosis. The endothelial cell dysfunction, which can lead to inhibition of fibrinolysis and excessive thrombin production, plays an important role in the occurrence of thrombotic events.[27] In addition, COVID-19 prepares the ground for thromboembolism through many mechanisms, such as cytokine storm and hypoxia.[28] These may explain why ischemic stroke is more common in COVID-19 patients compared to other stroke types.

In a systematic review and meta-analysis investigating the characteristics and outcomes of COVID-19-positive stroke patients, it has been reported that COVID-19-positive stroke patients are younger, males are affected to a greater degree, and hypertension is less common compared to non-COVID-19 stroke patients. In addition, no significant difference was found in terms of previous stroke, diabetes mellitus, dyslipidemia, smoking, coronary artery disease and atrial fibrillation, while these patients had higher in-hospital mortality.[29]

In another systematic review and meta-analysis comparing COVID-19-positive stroke patients with COVID-19-negative stroke patients, diabetes mellitus was reported to be more common in stroke patients with COVID-19 positivity.[30]

In our study, there was no significant difference in terms of age and sex in COVID-19-positive stroke patients compared to the COVID-19-negative stroke group. The percentage of kidney disease in the positive group was significantly higher than in the negative group (p=0.009). In a systematic review and meta-analysis examining the incidence and outcomes of COVID-19 in patients with chronic kidney disease, it was reported that these patients were at a higher risk of having COVID-19 and had a higher risk of death due to COVID-19 compared to the general population.[31] The groups had no significant difference regarding the frequency of other vascular risk factors.

It has been reported that there was a decrease in applications for acute stroke during the COVID-19 pandemic.[32-34] Our study found that the number of stroke cases hospitalised in our hospital during the COVID-19 pandemic was significantly reduced compared to the pre-pandemic period. In addition, the number of ischemic stroke and transient ischemic attack cases was substantially lower during the pandemic compared to the pre-pandemic period.

There could be many reasons for this outcome. Possible reasons leading to these results include curfews, the fact that stroke patients (particularly those with mild symptoms and clinical findings) could be refraining from applying to the hospital due to fear of exposure to COVID-19-infected individuals, the hospitals' distance from the city centre, higher selectivity regarding hospitalisation indications during the pandemic period, decreased bed count due to our institution being defined as a 'pandemic hospital', and decreases in the number of physicians working at the hospital.

There was no significant difference between the pre- and post-pandemic periods in intracranial haemorrhage and the number of patients hospitalised in the intensive care unit. Since intracranial haemorrhages are clinically more severe than ischemic strokes35, these patients may be admitted to the hospital more frequently. Therefore, the number of intracranial haemorrhage cases and severe patients requiring intensive care may not have changed significantly.

Study limitations

We cannot generalise our results due to various reasons, including the fact that this was a single-centre study conducted in the early stage of the pandemic, the number of our cases was limited, and it was conducted in a tertiary institution with a specialised stroke centre which was publically defined as a 'pandemic hospital'. Due to the risk of transmission in COVID-19 patients, detailed histories may not have been obtained, and detailed neurological examinations may not have been performed. In addition, the study included patients with informed consent from stroke patients with and without COVID-19 positivity between December 17, 2020 and January 31, 2021. Not including all stroke patients hospitalised in the same period may have affected the study results.

CONCLUSIONS

Our study observed that the number of stroke patients hospitalised during the pandemic period decreased. The majority of our patients were diagnosed with COVID-19 after admission to the hospital due to stroke. For this reason, it should be kept in mind that patients who apply to the hospital with stroke symptoms during the pandemic period may have COVID-19 even if they are asymptomatic, and, if possible, COVID-19 testing should be performed.

In addition, for patients diagnosed with COVID-19, attention should be paid to the possible signs and symptoms of stroke.

Conflict of Interest

No conflict of interest was declared by the authors.

Financial Disclosure

The authors declare that this study received no financial support.

Ethical Approval

Our study was approved by the Clinical Research Ethics Committee of Bursa City Hospital (decision number: 2020-12/1, date: 16.12.2020).

Authors' Contribution

Study Conception: HB., CH., MB.; Study Design: CH., HB., MB.; Supervision: HB., CH., MB.; Funding: HB., CH., MB.; Materials: HB., CH., MB.; Data Collection and/or Processing: HB., CH., MB.; Statistical Analysis and/or Data Interpretation: HB., CH., MB.; Literature Review: CH., HB., MB.; Manuscript Preparation: HB., CH., MB. and Critical Review: HB., CH., MB.

REFERENCES

1. Delorme C, Paccoud O, Kas A, Hesters A, Bombois S, Shambrook P, Boullet A, Doukhi D, Le Guennec L, Godefroy N, Maatoug R, Fossati P, Millet B, Navarro V, Bruneteau G, Demeret S, Pourcher V; CoCo-Neurosciences study group and COVID SMIT PSL study group. COVID-19-related encephalopathy: a case series with brain FDG-positron-emission tomography/computed tomography findings. Eur J Neurol. 2020 Dec;27(12):2651-7. doi: 10.1111/ene.14478.
2. Zambreanu L, Lightbody S, Bhandari M, Hoskote C, Kandil H, Houlihan CF, Lunn MP. A case of limbic encephalitis associated with asymptomatic COVID-19 infection. J Neurol Neurosurg Psychiatry. 2020 Nov;91(11):1229-30. doi: 10.1136/jnnp-2020-323839.
3. Khoo A, McLoughlin B, Cheema S, Weil RS, Lambert C, Manji H, Zandi MS, Morrow JM. Postinfectious brainstem encephalitis associated with SARS-CoV-2. J Neurol Neurosurg Psychiatry. 2020 Sep;91(9):1013-1014. doi: 10.1136/jnnp-2020-323816.
4. Durmaz ŞE, Kaya BU, Gümüşyayla Ş. Association Between Guillain-Barré Syndrome and COVID-19 Infection: Experience of a Turkish Neurophysiology Laboratory. Noro Psikiyatr Ars. 2022 Nov 7;59(4):255-9. doi: 10.29399/npa.27855.
5. Türk Börü Ü, Köseoğlu Toksoy C, Bölük C, Demirbaş H, Yılmaz AÇ. A case of Guillain-Barré syndrome related to COVID-19 infection. Int J Neurosci. 2023 Jan;133(1):86-8. doi: 10.1080/00207454.2021.1886097.
6. Chang S, Schecht M, Jain R, Belani P. Acute neurological complications of coronavirus disease. Neuroimaging Clin N Am. 2023 Feb;33(1):57-68. doi: 10.1016/j.nic.2022.07.003.
7. Czarnowska A, Zajkowska J, Kułakowska A. Impact of SARS-CoV-2 on the nervous system. Neurol Neurochir Pol. 2023;57(1):26-35. doi: 10.5603/PJNNS.a2023.0009.
8. Usta NC, Kartal S, Gunay BO, Boz C. Neurological manifestations and etiological risk factors in patients hospitalized with COVID-19 in Turkey. Asian Biomed (Res Rev News). 2022 Feb 28;16(1):23-30. doi: 10.2478/abm-2022-0004.
9. Alay H, Can FK, Gözgeç E. Cerebral infarction in an elderly patient with coronavirus disease. Rev Soc Bras Med Trop. 2020 Jun 3;53:e20200307. doi: 10.1590/0037-8682-0307-2020.
10. Hernández-Fernández F, Sandoval Valencia H, Barbella-Aponte RA, Collado-Jiménez R, Ayo-Martín Ó, Barrena C, Molina-Nuevo JD, García-García J, Lozano-Setién E, Alcahut-Rodriguez C, Martínez-Martín Á, Sánchez-López A, Segura T. Cerebrovascular disease in patients with COVID-19: neuroimaging, histological and clinical description. Brain. 2020 Oct 1;143(10):3089-103. doi: 10.1093/brain/awaa239.
11. Finsterer J, Scorza FA, Scorza CA, Fiorini AC. Ischemic stroke in 455 COVID-19 patients. Clinics (Sao Paulo). 2022 Feb 14:77:100012. doi: 10.1016/j.clinsp.2022.100012.
12. Dallas J, Liu KQ, Wenger TA, Lin M, Ding L, Attenello FJ, Mack WJ. The effect of COVID-19 on treatment and outcomes following ischemic stroke: A national assessment. Clin Neurol Neurosurg. 2023 Oct;233:107982. doi: 10.1016/j.clineuro.2023.107982.
13. Görgülü Ü, Şahin MH, Bektaş H. Acute stroke in Covid-19 infection: Neurology intensive care experience. Süleyman Demirel Üniversitesi Sağlık Bilimleri Dergisi. 2022;13(1):111-8 (in Turkish). Doi: 10.22312/sdusbed.1069267.
14. Luo W, Liu X, Bao K, Huang C. Ischemic stroke associated with COVID-19: a systematic review and meta-analysis. J Neurol. 2022 Apr;269(4):1731-40. doi: 10.1007/s00415-021-10837-7.
15. Pourciau P, Smith BC. Stroke risk related to coronavirus disease-2019: What have we learned? Crit Care Nurs Clin North Am. 2023 Mar;35(1):53-65. doi: 10.1016/j.cnc.2022.10.001.
16. Demirelli DS, Genc G, Basarir CI, Bulut S. Comparison of clinical characteristics of COVID-19-related and unrelated acute stroke patients during the COVID-19 pandemic in Turkey. Sisli Etfal Hastan Tip Bul. 2022 Mar 28;56(1):55-61.

doi: 10.14744/SEMB.2021.65785.
17. Cerón Blanco N, Romero Hernández CA, Vallejo Fernández J. Acute stroke in COVID-19 patients: A first year experience in a Colombian hospital. Neurol Perspect. 2023 Apr-Jun;3(2):100121. doi: 10.1016/j.neurop.2023.100121.
18. Benny R, Singh RK, Venkitachalam A, Lalla RS, Pandit RA, Panchal KC, Pardasani V, Chanchalani G, Basle M, Bolegave V, Manoj H, Shetty AN, Shah AM, Pai P, Banthia NM, Patil SG, Chafale V, Pujara B, Shah S, Mehta N, Thakkar VV, Patel V, Shetty KV. Characteristics and outcomes of 100 consecutive patients with acute stroke and COVID-19. J Neurol Sci. 2021 Apr 15;423:117348. doi: 10.1016/j.jns.2021.117348.
19. García-Moncó JC, Cabrera-Muras A, Collía-Fernández A, Erburu-Iriarte M, Rodrigo-Armenteros P, Oyarzun-Irazu I, Martínez-Condor D, Bilbao-González A, Carmona-Abellán M, Caballero-Romero I, Gómez-Beldarrain M. Neurological reasons for consultation and hospitalization during the COVID-19 pandemic. Neurol Sci. 2020 Nov;41(11):3031-8. doi: 10.1007/s10072-020-04714-w.
20. Oliveira IB, Pessoa MS, Lima CF, Holanda JL, Coimbra PPA. Ischaemic stroke as an initial presentation in patients with COVID-19: evaluation of a case series in an emergency in Brazil. Neuroradiol J. 2021 Aug;34(4):308-12. doi: 10.1177/1971400920987357.
21. Tan YJ, Narasimhalu K, Chan Y, De Silva DA. Stroke patients without COVID-19 symptoms: Is there a need to screen? Neurologist. 2021 Mar 4;26(2):73-4. doi: 10.1097/NRL.0000000000000305.
22. Tunç A, Ünlübaş Y, Alemdar M, Akyüz E. Coexistence of COVID-19 and acute ischemic stroke report of four cases. J Clin Neurosci. 2020 Jul:77:227-9. doi: 10.1016/j.jocn.2020.05.018.
23. Davis MG, Gangu K, Suriya S, Maringanti BS, Chourasia P, Bobba A, Tripathi A, Avula SR, Shekhar R, Sheikh AB. COVID-19 and acute ischemic stroke mortality and clinical outcomes among hospitalized patients in the United States: Insight from national inpatient sample. J Clin Med. 2023 Feb 8;12(4):1340. doi: 10.3390/jcm12041340.
24. Ferrone SR, Sanmartin MX, Ohara J, Jimenez JC, Feizullayeva C, Lodato Z, Shahsavarani S, Lacher G, Demissie S, Vialet JM, White TG, Wang JJ, Katz JM, Sanelli PC. Acute ischemic stroke outcomes in patients with COVID-19: a systematic review and meta-analysis. J Neurointerv Surg. 2024 Mar 14;16(4):333-341. doi: 10.1136/jnis-2023-020489.
25. Siow I, Lee KS, Zhang JJY, Saffari SE, Ng A, Young B. Stroke as a neurological complication of COVID-19: A systematic review and meta-analysis of incidence, outcomes and predictors. J Stroke Cerebrovasc Dis. 2021 Mar;30(3):105549. doi: 10.1016/j.jstrokecerebrovasdis.2020.105549.
26. Topcuoglu MA, Pektezel MY, Oge DD, Bulut Yüksel ND, Ayvacioglu C, Demirel E, Balci S, Arat A, Akinci SB, Arsava EM. Stroke mechanism in COVID-19 infection: A prospective case-control study. J Stroke Cerebrovasc Dis. 2021 Aug;30(8):105919. doi: 10.1016/j.jstrokecerebrovasdis.2021.105919.
27. Li S, Ren J, Hou H, Han X, Xu J, Duan G, Wang Y, Yang H. The association between stroke and COVID-19-related mortality: a systematic review and meta-analysis based on adjusted effect estimates. Neurol Sci. 2022 Jul;43(7):4049-59. doi: 10.1007/s10072-022-06024-9.
28. May B, Wang DZ. Coronavirus disease 2019 infection and cerebrovascular diseases: an update on the pathophysiology and management. Curr Opin Neurol. 2023 Apr 1;36(2):155-64. doi: 10.1097/WCO.0000000000001146.
29. Nannoni S, De Groot R, Bell S, Markus HS. Stroke in COVID-19: A systematic review and meta-analysis. Int J Stroke. 2021 Feb;16(2):137-49. doi: 10.1177/1747493020972922.
30. Katsanos AH, Palaiodimou L, Zand R, Yaghi S, Kamel H, Navi BB, Turc G, Romoli M, Sharma VK, Mavridis D, Shahjouei S, Catanese L, Shoamanesh A, Vadikolias K, Tsioufis K, Lagiou P, Alexandrov AV, Tsiodras S, Tsivgoulis G. The impact of SARS-CoV-2 on stroke epidemiology and care: A Meta-Analysis. Ann Neurol. 2021 Feb;89(2):380-8. doi: 10.1002/ana.25967.
31. Chung EYM, Palmer SC, Natale P, Krishnan A, Cooper TE, Saglimbene VM, Ruospo M, Au E, Jayanti S, Liang A, Jie Deng DJ, Chui J, Higgins GY, Tong A, Wong G, Teixeira-Pinto A, Hodson EM, Craig JC, Strippoli GFM. Incidence and outcomes of COVID-19 in people with CKD: A systematic review and meta-analysis. Am J Kidney Dis. 2021 Dec;78(6):804-15. doi: 10.1053/j.ajkd.2021.07.003.
32. Gunnarsson K, Tofiq A, Mathew A, Cao Y, von Euler M, Ström JO. Changes in stroke and TIA admissions during the COVID-19 pandemic: A meta-analysis. Eur Stroke J. 2024 Mar;9(1):78-87. doi: 10.1177/23969873231204127.
33. Padroni M, Laudisi M, Azzini C, De Vito A, Casetta I. Stroke admissions during the COVID-19 pandemic: a single-center retrospective analysis. Neurol Sci. 2022 Sep;43(9):5169-74. doi: 10.1007/s10072-022-06207-4.
34. Nguyen TN, Qureshi MM, Klein P, Yamagami H, Mikulik R, Czlonkowska A, Abdalkader M, Sedova P, Sathya A, Lo HC, Mansour OY, Vanguru HR, Lesaine E, Tsivgoulis G, Loochtan AI, Demeestere J, Uchino K, Inoa V, Goyal N, Charidimou A, Siegler JE, Yaghi S, Aguiar de Sousa D, Mohammaden MH, Haussen DC, Kristoffersen ES, Lereis VP, Scollo SD, Campbell BCV, Ma A, Thomas JO, Parsons MW, Singhal S, Slater LA, Tomazini Martins

R, Enzinger C, Gattringer T, Rahman A, Bonnet T, Ligot N, De Raedt S, Lemmens R, Vanacker P, Vandervorst F, Conforto AB, Hidalgo RCT, de Oliveira Neves L, Martins RT, Mora Cuervo DL, Rebello LC, Santiago IB, Lameirinhas da Silva I, Sakelarova T, Kalpachki R, Alexiev F, Catanese L, Cora EA, Goyal M, Hill MD, Kelly ME, Khosravani H, Lavoie P, Peeling L, Pikula A, Rivera R, Chen HS, Chen Y, Huo X, Miao Z, Yang S, Bedekovic MR, Bralic M, Budincevic H, Corredor-Quintero AB, Lara-Sarabia OE, Cabal M, Tenora D, Fibrich P, Herzig R, Hlaváčová H, Hrabanovska E, Hlinovsky D, Jurak L, Kadlcikova J, Karpowicz I, Klecka L, Kovar M, Lauer D, Neumann J, Palouskova H, Reiser M, Rekova P, Rohan V, Skoda O, Škorňa M, Sobotková L, Sramek M, Zakova L, Christensen H, Drenck N, Iversen HK, Truelsen TC, Wienecke T, Sobh K, Ylikotila P, Alpay K, Strbian D, Bernady P, Casenave P, Dan M, Faucheux JM, Gentric JC, Magro E, Sabben C, Reiner P, Rouanet F, Bohmann FO, Boskamp S, Mbroh J, Nagel S, Nolte CH, Ringleb PA, Rosenkranz M, Poli S, Thomalla G, Karapanayiotides T, Koutroulou I, Kargiotis O, Palaiodimou L, Barrientos Guerra JD, Huded V, Menon B, Nagendra S, Prajapati C, Sylaja PN, Krishna Pramana NA, Sani AF, Ghoreishi A, Farhoudi M, Hokmabadi ES, Raya TA, Kalmanovich SA, Ronen L, Sabetay SI, Acampa M, Adami A, Castellan L, Longoni M, Ornello R, Renieri L, Bigliani CR, Romoli M, Sacco S, Salmaggi A, Sangalli D, Zini A, Doijiri R, Fukuda H, Fujinaka T, Fujita K, Imamura H, Sakai N, Kanamaru T, Kimura N, Kono R, Miyake K, Sakaguchi M, Sakai K, Sonoda K, Todo K, Miyashita F, Tokuda N, Matsumaru Y, Matsumoto S, Ohara N, Shindo S, Takenobu Y, Yoshimoto T, Toyoda K, Uwatoko T, Yagita Y, Yamada T, Yamamoto N, Yamamoto R, Yazawa Y, Sugiura Y, Waweru PK, Baek JH, Lee SB, Seo KD, Sohn SI, Arsovska AA, Chan YC, Wan Zaidi WA, Jaafar AS, Gongora-Rivera F, Martinez-Marino M, Infante-Valenzuela A, Groppa S, Leahu P, Coutinho JM, Rinkel LA, Dippel DWJ, van Dam-Nolen DHK, Ranta A, Wu TY, Adebayo TT, Bello AH, Nwazor EO, Sunmonu TA, Wahab KW, Ronning OM, Sandset EC, Al Hashmi AM, Ahmad S, Rashid U, Rodriguez-Kadota L, Vences MÁ, Yalung PM, Hao Dy JS, Pineda-Franks MC, Co CO, Brola W, Debiec A, Dorobek M, Karlinski MA, Labuz-Roszak BM, Lasek-Bal A, Sienkiewicz-Jarosz H, Staszewski J, Sobolewski P, Wiacek M, Zielinska-Turek J, Araujo AP, Rocha M, Castro P, Cruz VT, Ferreira PV, Ferreira P, Nunes AP, Fonseca L, Marto JP, Pinho E Melo T, Rodrigues M, Silva ML, Dimitriade A, Falup-Pecurariu C, Hamid MA, Venketasubramanian N, Krastev G, Mako M, Ayo-Martin O, Hernández-Fernández F, Blasco J, Rodríguez-Vázquez A, Cruz-Culebras A, Moniche F, Montaner J, Perez-Sanchez S, García Sánchez MJ, Guillán Rodríguez M, Jood K, Nordanstig A, Mazya MV, Moreira TTP, Bernava G, Beyeler M, Bolognese M, Carrera E, Dobrocky T, Karwacki GM, Keller E, Hsieh CY, Boonyakarnkul S, Churojana A, Aykac O, Ozdemir AÃ, Bajrami A, Senadim S, Hussain SI, John S, Banerjee S, Kwan J, Krishnan K, Lenthall R, Matthews A, Wong K, Zhang L, Altschul D, Asif KS, Bahiru Z, Below K, Biller J, Ruland S, Chaudry SA, Chen M, Chebl A, Cibulka J, Cistrunk L, Clark J, Colasurdo M, Czap A, de Havenon A, D'Amato S, Dharmadhikari S, Grimmett KB, Dmytriw AA, Etherton MR, Ezepue C, Farooqui M, Feske SK, Fink L, Gasimova U, Guzik AK, Hakemi M, Hovingh M, Khan M, Jillela D, Kan PT, Khatri R, Khawaja AM, Khoury NN, Kiley NL, Kim BS, Kolikonda MK, Kuhn AL, Lara S, Linares G, Linfante I, Lukovits TG, Lycan S, Male SS, Maali L, Mancin J, Masoud H, Mohamed GA, Monteiro A, Nahab F, Nalleballe K, Ortega-Gutierrez S, Puri AS, Radaideh Y, Rahangdale RH, Rai A, Ramakrishnan P, Reddy AB, Rojas-Soto DM, Romero JR, Rost NS, Rothstein A, Omran SS, Sheth SA, Siddiqui AH, Starosciak AK, Tarlov NE, Taylor RA, Wang MJ, Wolfe J, Wong KH, Le HV, Nguyen QV, Pham TN, Nguyen TT, Phan HT, Ton MD, Fischer U, Michel P, Strambo D, Martins SO, Zaidat OO, Nogueira RG; and the SVIN COVID-19 Global Stroke Registry. Global impact of the COVID-19 pandemic on stroke volumes and cerebrovascular events: a 1-year follow-up. Neurology. 2023 Jan 24;100(4):e408-e421. doi: 10.1212/WNL.0000000000201426.
35. Andersen KK, Olsen TS, Dehlendorff C, Kammersgaard LP. Hemorrhagic and ischemic strokes compared: stroke severity, mortality, and risk factors. Stroke. 2009 Jun;40(6):2068-72. doi: 10.1161/STROKEAHA.108.540112.