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Original article

Risk of Stroke in Hospitalized SARS-Cov-2 Infected Patients

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Abstract

Background: Stroke is one of the most common and fatal neurologic abnormalities. Multiple risk factors, including smoking, hypertension, diabetes and hyperlipidemia, can lead to a stroke. **This study aimed to** estimate the stroke short-term risk and its associated factors among SARS-CoV-2 hospitalized cases. **Methods:** This cross-sectional comparison groups was conducted on SARS-CoV-2 infected patients in two phases: Phase 1: cross sectional study in which the prevalence of stroke could be estimated. Phase 2: grouping among the study population in order to find out different risk factors. All patients underwent medical history taking, full general and neurological examinations, PCR or chest CT scan screening, brain CT scan and Canadian Neurological Scale **Results**: There was no significant correlation between the stroke different types and risk factors. There was an insignificant correlation between stroke severity and risk factors. There was no statistically significant difference in stroke severity; assessed by Canadian neurological scale; between different stroke types. **Conclusion:** We detected a low incidence of imaging-confirmed ischemic stroke in hospitalized COVID- 19-infected individuals. Mild, Moderate, and Severe on the Canadian neurological scale were unrelated to the observed results (AIS, ICH, and CVT).

Keywords: Stroke; Hospitalized; SARS-CoV-2; Infected Patients

Introduction

The World Health Organization defines a stroke as a clinical disorder characterized by quickly developing clinical signs of localized impairment of brain function, lasting more

than 24 hours, or concluding in death with no other clear cause than vascular origin (1).

Stroke is one of the most prevalent and lethal neurologic disorders. A stroke can be caused by several risk factors, including smoking, hypertension, diabetes, and hyperlipidemia (2).

A number of cerebrovascular incidents in SARS-CoV-2 patients have been observed since the publication of COVID-19. In SARS-CoV-2–infected patients, researchers studied the frequency and prevalence of acute ischemic stroke (AIS), intracranial hemorrhage (ICH), and cerebral venous or sinus thrombosis (3).

Numerous studies suggest that the pathophysiological root cause of cerebrovascular episodes is coagulopathy. In limited case series, SARS-CoV-2 infection was associated with an increased risk of severe arterial occlusions or cryptogenic strokes, as well as raised levels of liver enzymes, D-dimer, and renal failure or inflammatory biomarkers. In addition, the majority of studies discovered that SARS-CoV-2-positive stroke patients had a greater risk of death and stroke severity than other patients (4).

The study's goal was to estimate the stroke short-term risk and its associated factors among SARS-CoV-2 hospitalized patients.

Patients and methods

This cross-sectional comparison groups was conducted on SARS-CoV-2 infected patients in two phases: Phase 1: cross sectional study in which the prevalence of stroke could be estimated. Phase 2: grouping among the study population in order to find out different risk factors. The study period was from November 2021 till September 2022.

This study was conducted at Benha University Hospital & October 6 university hospital. The study was conducted after receiving approval from the Benha University research ethics committee. The approval number of the local ethical committee: **MS.29.1.2021**

Inclusion criteria were hospitalized SARS-CoV-2 cases who had an ICH, a subsequent and confirmed stroke—ischemic stroke, subarachnoid hemorrhage, and CVT. Patients who were first presented to the hospital with a stroke-related complaint, were diagnosed with an imaging-confirmed acute stroke, but also had positive SARS2-CoV-2 screening results. Patients have been hospitalized for over 24 hours.

Exclusion criteria were transient stroke-like symptoms and no acute lesion on MRI or CT.

Operational design: The eligible patients underwent **full history** including personal data and comorbidities. **Physical examination** including general and clinical examinations. **ECG and laboratory investigations.**

Quantitative reverse transcription polymerase chain reaction: Viral RNAs were isolated from the samples using the QIAamp RNA Viral Kit, and quantitative reverse transcription polymerase chain reaction was done using a commercial kit certified by the China Food and Drug Administration for the detection of 2019-nCoV. (GeneoDX Co., Ltd., Shanghai, China). Positive specimens have a Ct value below 37,0 and negative specimens have equivocal data. Samples having a Ct value of at least 37 are repeated. If the repeat readings conform to the first result and fall between 37 to 40, the drug is considered positive. If the repeat Ct cannot be detected, the sample is considered negative. The retesting of a patient who has had several RT-PCR tests within three days of the initial test is diagnostic confirmation. The conversion of RT-PCR data was examined in conjunction with a chest CT scan by repeating the test more than three days after the initial test.

Chest CT protocols and Image analysis: All images are obtained with patients in supine position. All chest CT images are analyzed and graded as positive or negative based on a consensus, but RT-PCR findings are concealed.

CT scan of the brain: Cranial CT was done by using Toshiba (Activion 16) with 11.3 scanning time and 265 x 265 matrix size. Axial scans were obtained with the patient supine, and the slice thickness was 3 mm. The classification of a hemorrhagic stroke was either ICH or non-aneurysmal SAH. Hypertension, coagulopathy, brain metastases, vascular abnormalities (arteriovenous malformation) were identified as the cause of the bleeding. ICH was classified as mostly deep, predominantly cortical, both deep and cortical, or multifocal.

Patients' initial stroke severity was evaluated on admission by the Canadian Neurological Scale (5).

The Canadian Neurological Scale consists of eight tests used to evaluate awareness, orientation, speech, motor function, and facial weakness. CNS monitoring must be conducted whether the patient is awake or

asleep (sections A1 and A2). Using the Glasgow Coma Scale, observe the patient if he or she is stupefied or comatose.

Mentation: level of consciousness: Alert 3.0 Normal eyelid opening and level of awareness the patient remains alert and attentive when spoken stimulated but tends to nod asleep.

ECG: 12-lead ECGs were obtained at the time of admission (Cardiovit AT-60; Schiller, Switzerland). Throughout the first 12–24 hours after admission, continuous ECG telemetry (Teleguard 3200; Danica Biomedical A/S, Denmark) was done.

Laboratory testing: About 5 ml blood volume was withdrawn from each participant once. Blood sugar level, liver and kidney function tests, lipid and coagulation profile, CBC, CRP, serum ferritin and D-dimer.

Statistical analysis

Version v28 of SPSS was used for statistical analysis (IBM Inc., Armonk, NY, USA). Using an unpaired Student's t-test, mean and standard deviation (SD) were provided to represent the quantitative data. Chi-square test was utilized to evaluate qualitative data and frequency and percentage (%) expressed these data. Pearson correlation coefficient was also estimated. P-value (two-tailed) less than 0.05 was considered significant.

Results

The study group included 60 cases: 29 females (48.3%) and 31 males (51.7%). Their age had a mean value of 61.40±11.87 years. 63.3% of our cases had hypertension, 38.3% had Diabetes Mellitus, 35.0% had Cardiac Disease, 63.3% had Hyperlipidemia, 30.0% had Prior stroke and 20.0% were smokers. 71.7% and 25% of the studied cases had AIS and intracranial hemorrhage respectively as outcome. CVT was reported in 2 cases (3.3%) only.

33, 17 and 10 patients (55%, 28.3% and 16.7%) had mild stroke, moderate stroke and severe stroke respectively according to the Canadian neurological scale. Their mean ± SD scores were 8.70 ± 0.40, 6.21 ± 0.68 and 3.41 ± 0.65 respectively. **Table 1**

All studied cases had abnormally higher levels of inflammatory markers (CRP, D-dimer) while only 63.3% of them had abnormal INR. 71.7% and 91.7% of our patients had abnormal serum levels of blood urea and creatinine respectively. Abnormal Neutrophilic count was detected in 86.7% of our cases. **Table 2**

CRP and D-dimer were insignificantly different between different stroke severities. **Table 3**

There was no significant difference in stroke severity; assessed by Canadian neurological scale; between different stroke types. **Table 4**

Table 1: Stroke severity in the studied cases evaluated by the Canadian neurological scale

Stroke severity	Study group (n=60)		Scores of Canadian neurological scale		
	No.	**%**	**Range**	**Mean ± SD.**	**Median (IQR)**
Mild	33	55.0	8.10 – 9.50	8.70 ± 0.40	8.70 (8.40 – 8.90)
Moderate	17	28.3	5.20 – 7.0	6.21 ± 0.68	6.50 (5.40 – 6.80)
Severe	10	16.7	2.60 – 4.0	3.41 ± 0.65	3.65 (2.70 – 4.0)
Total	60	100.0	2.60 – 9.50	7.11 ± 2.06	8.15 (5.6 – 8.7)

IQR: Inter quartile range, SD: Standard deviation

Table 2: Laboratory investigations of the studied cases

Parameter	Study group (n=60)	
	Cases with Normal findings	**Cases with Abnormal findings**
WBCs ($\times10^9$/L)	31 (51.7%)	29 (48.3%)
Neutrophil count ($\times10^9$/L)	8 (13.3%)	52 (86.7%)
Lymphocyte count ($\times10^9$/L)	32 (53.3%)	28 (46.7%)
PLTs ($\times10^9$/L)	43 (71.7%)	17 (28.3%)
ALT (U/L)	30 (50.0%)	30 (50.0%)
AST (U/L)	29 (48.3%)	31 (51.7%)
BUN (mg/dl)	17 (28.3%)	43 (71.7%)
Creatinine (mg/dl)	5 (8.3%)	55 (91.7%)
CRP (mg/l)	0 (0.0%)	60(100.0%)
D-dimer	0 (0.0%)	60(100.0%)
INR	22 (36.7%)	38 (63.3%)

Table 3: Correlation between stroke severity and inflammatory markers (CRP and D-dimer) in the studied cases

Inflammatory marker	Study group (n =60) Canadian neurological scale				
	Mild (n = 33)	**Moderate (n = 17)**	**Severe (n = 10)**	**H**	**p**
CRP (mg/l)					
Mean ± SD	68.06 ± 53.93	67.31 ± 59.92	66.44 ± 59.98		
Median (range)	48.40 (7.0 – 167.2)	61.30 (6.70 – 164.0)	55.40 (5.60 – 156.9)	0.059	0.971
D-dimer					
Mean ± SD	1.43 ± 0.63	1.28 ± 0.54	1.44 ± 0.66	0.504	0.777
Median (range)	1.32 (0.63 – 2.87)	1.27 (0.50 – 2.27)	1.17 (0.80 – 2.56)		

SD: **Standard deviation,** H: H for **Kruskal Wallis test,** p: p value for Relation between Canadian neurological scale with CRP and D-dimer, $p<0.05$ is significant.

Table 4: Correlation between stroke severity (assessed by Canadian neurological scale) and stroke type

Stroke type	Study group (n = 60)						χ^2	^{MC}p
	Stroke severity							
	Mild (n = 33)		Moderate (n = 17)		Severe (n = 10)			
	No.	%	No.	%	No.	%		
Acute ischemic stroke	23	69.7	12	70.6	8	80.0	4.453	0.304
Intracranial Hemorrhage	10	30.3	4	23.5	1	10.0		
Cerebral venous thrombosis	0	0.0	1	5.9	1	10.0		

χ^2: **Chi square test**, MC: **Monte Carlo,** p: p value for Relation between outcome with risk factors, P<0.05 is significant.

Discussion

In the present study, 43(71.7%) had AIS, 15(25.0%) had Intracranial Hemorrhage, 2(3.3%) had CVT.

Similar to our findings, a study recorded patients who had a subsequent and confirmed stroke, ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage, and CVT and found among the 156 stroke patients, intracerebral/subarachnoid hemorrhage were found in 27 (17%), AIS were presented in 123 (79%), and CVST were found in 6 (4%) and of 32 patients the reason of admission was (stroke in 43.8%, and COVID-19 symptoms in 56.2%, with index stroke occurring during the hospital stay) (6).

It was determined in a systematic review that the vast majority of strokes among COVID-19 patients were arterial stroke (98.5%), whereas just three patients had venous stroke (1.5%). Contrary to the 9.7% of patients who presented with a hemorrhagic stroke, 90.3% of all stroke cases were due to an ischemic stroke. 60% of strokes occurred in the anterior circulation, followed by a number of places (28%) and the posterior circulation (28%). Only two of the 29 cases of anterior circulation-related stroke were associated with the area of the anterior cerebral artery (7).

According to Canadian neurological scale, 33(55.0%) of cases had Mild Canadian neurological scale with a mean ± SD value of 8.70 ± 0.40, 17(28.3%) had Moderate Canadian neurological scale ranged from 8.10 – 9.50.

A study revealed that the median (IQR) of NIHSS at admission was 12.5 (15.8) (n=170) and 44.2% (87/197) of the patients presented with LVO (8). Individuals with intracerebral/subarachnoid hemorrhage had an NIHSS of 13 [8.0–17.0] and an ICH score of 3.0 [2.0–4.0] in the research another

research conducted. Twenty-five patients (93%) had ICH, while two patients (7%) suffered subarachnoid hemorrhage. Two (33%) of the six patients with CVT had seizures prior to admission (6).

According to Canadian neurological scale, mean ± SD value of 6.21 ± 0.68, and 10 (16.7%) had Severe Canadian neurological scale ranged from 2.60 – 4.0 with a Mean (±SD) value of 3.41 ± 0.65.

In a study, it was found that Milder stroke severity was observed in the COVID-19 period (NIHSS 6 [2–20] vs. 3 [2–15], p = 0.005) (9).

Our present study, there was an insignificant relationship between outcome (AIS, ICH, and CVT) and both risk factors (HTN, Cardiac Disease, DM, Prior stroke, Hyperlipidemia, Smoking) and Canadian neurological scale Mild, Moderate, and Severe. Our study showed that There was an insignificant relationship between Canadian neurological scale Mild, Moderate, and Severe and Risk factors (DM, Cardiac Disease, HTN, Hyperlipidemia, smoking, prior stroke and CRP and D-dimer).

In contrast with our results, a study reported that advanced age (more than 60), DM, higher NLR, higher admission NIHSS, LVO presence and occurrence of sICH as poor outcomes predictors (8).

In a study, it was discovered that there was no association between inflammatory indicators and hypercoagulability. This is an intriguing discovery not previously discussed in COVID-19 stroke or hypercoagulability research (8). This may explain why higher prophylactic anticoagulation targets may not have decreased mortality in a significant proportion of COVID-19-associated individuals (10).

Conclusion

We observed a relatively low incidence of imaging-confirmed ischemic stroke in COVID- 19-infected hospitalized patients. Mild, Moderate, and Severe on the Canadian neurological scale were not associated with the outcomes (AIS, ICH, and CVT).

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