Cross-sectional Study

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Stroke patterns and outcomes during the second wave of COVID-19 pandemic: a cross-sectional study

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Background: The coronavirus disease 2019 (COVID-19) pandemic has affected the number of stroke activations, admission of patients with various types of strokes, the rate and timely administration of reperfusion therapy, and all types of time-based stroke-related quality assessment metrics. In this study, we describe the different types of strokes, different delays in seeking and completing treatment occurring during the second wave of the COVID-19 pandemic, and predictors of outcome at 3 months follow-up.

Materials and methods: This is a single-centered prospective cross-sectional study carried out from May 2021 to November 2021, enrolling patients with stroke. Data collected were demographic characteristics, stroke types and their outcomes, and different types of prehospital delays.

Results: A total of 64 participants were included in the study with a mean age of 60.25 ± 15.31 years. Ischemic stroke was more common than hemorrhagic stroke. The median time of arrival to the emergency room of our center was 24 h. The most common cause of prehospital delay was found to be delays in arranging vehicles. The median duration of hospital stays [odds ratio (OR) = 0.72, $P < 0.05$] and baseline NIHSS (National Institute of Health Stroke Scale) score (OR = 0.72, $P < 0.05$) were found to be a predictor of good outcomes at 3 months follow-up on binary logistic regression.

Conclusion: The factors that cause the delayed transfer to the hospital and onset of treatment should be addressed. Patient counseling about the likely prognosis can be done after evaluating the probable outcome based on the NIHSS score and median duration of hospital stay. Nevertheless, mechanisms should be developed to reduce the prehospital delay at the ground level as well as at the policy level.

Keywords: COVID-19, hemorrhagic stroke, ischemic stroke, LMIC, NIHSS, prehospital delay

Introduction

With the emergence and spread of the novel coronavirus and mandatory lockdowns enforced throughout the world during 2020 and 2021, health-seeking behavior and response to it have been severely affected throughout the world[1]. Stroke care has not been an exception[2]. The coronavirus disease 2019 (COVID-19) pandemic has affected the number of stroke activations, admission of patients with various types of stroke, the rate and timely administration of reperfusion therapy, and all types of time-based stroke-related quality assessment metrics[3,4]. In addition to the reasons related to the delays attributed to imposed lockdowns and other logistic issues, the outcome of stroke during the pandemic has been adversely affected by the disease itself. COVID-19 itself causes severe stroke and poorer outcomes when compared with historical groups of patients[5,6].

A survey done by the Asian Stroke Advisory Panel (ASAP) showed the negative impact of the pandemic on the healthcare-seeking approach of stroke patients. The statistics demonstrate a fall in the number of stroke admissions and a decline in the number of patients receiving thrombolysis and mechanical thrombectomy across 13 institutions in 9 different Asian countries[7]. Similarly, there were higher in-hospital complications

HIGHLIGHTS

- The coronavirus disease 2019 (COVID-19) pandemic resulted in lower stroke admission rates, thrombolysis therapy rates, and severely affected time metrics in stroke care.
- Higher baseline NIHSS scores and longer duration of hospital stay were predictors of poor outcomes.
- Ensuring effective stroke treatment even in times of crisis like the COVID-19 pandemic should be a top priority.
- Mechanisms should be developed to reduce the prehospital delay at the ground level as well as at the policy level.

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and mortality, and mortality at 3 months among COVID-positive stroke patients, whereas a favorable outcome was observed among non-COVID patients in a multicentric study of stroke patients performed by the COVID-19 stroke study group (CSSG) of India during the pandemic[8].

To date, large-scale studies on the outcomes of stroke in Nepal are not available. In a small study conducted in central Nepal, the 3 months outcome of patients with ischemic stroke was 51.8% achieving full independence, 19.6% dependent, and 28.6% dead[9]. Likewise, there have been no studies on the outcomes of hemorrhagic stroke in 3 months in Nepal. In a prospective study carried out in a tertiary center in India, mortality was 30.1%, a favorable outcome was observed in 45.5% of patients, and a poor outcome in 22.87%[10].

In this study, we describe the different types of strokes and their outcomes occurring during the second wave of the COVID-19 pandemic. We also describe whether there were any delays in seeking and completing treatment and the factors contributing to such delays. Factors that may contribute to worse outcomes are identified. The study can be of significant value in understanding the impact of a months-long pandemic on stroke management and outcome and can be comparably used to relate the outcome of stroke to the pre-pandemic era.

Methods

This is a prospective observational study carried out on data collected from patients with acute stroke admitted to the medical wards of our university hospital, the largest tertiary care and referral center in Nepal, during the second wave of the COVID-19 pandemic (May 2021 to November 2021). Convenient sampling was used to include all patients aged 14 years or more who were admitted with the diagnosis of acute stroke. This study is reported according to STROCSS (strengthening the reporting of cohort, cross-sectional and case–control studies in surgery) 2021[11] criteria and registered in the research registry (researchregistry8397). A self-designed questionnaire was employed to collect the data. The demographic and clinical variables included in the questionnaire were age, sex, address (inside or outside valley), contact number, date of stroke onset, whether the onset was witnessed, type of stroke, time to present to the emergency room (ER), the impact of the pandemic on the time of arrival to ER and stroke treatment (thrombolysis and/or thrombectomy), COVID-19 status, neurological examination findings, progression of symptoms during the hospital stay, duration of hospital stay, whether the patient did regular physiotherapy at any physiotherapy center or at home, whether speech and dysphagia experts were met, whether the patient followed up after discharge until 3 months after discharge, and outcomes of the stroke at the third month. Patients who lived in Kathmandu, Bhaktapur, and Lalitpur districts were grouped into the address category 'inside the valley' and other patients were grouped into the address category 'outside the valley'. The stroke was broadly divided into ischemic, hemorrhagic, and cerebral venous sinus thrombosis. The ischemic stroke that we encountered was subdivided into large vessel occlusion (LVO) stroke, lacunar stroke, and embolic stroke. Likewise, hemorrhagic stroke was grouped into hypertensive hemorrhagic stroke and non-hypertensive hemorrhagic stroke. The National Institute of Health Stroke Scale (NIHSS) score was used to rate the severity of stroke on admission. The stroke severity was grouped into no stroke (NIHSS score 0), minor stroke (NIHSS score 1–4), moderate stroke (NIHSS score 5–15), moderate to severe stroke (NIHSS 16–20), and severe stroke (NIHSS score 21–42). The last category was not encountered in the study. The outcome of the patients was evaluated by using the Modified Rankin Scale (mRS) at 3 months when the patients came for follow-up in the outpatient department. Patients who could not come for follow-up were evaluated by using telephone interviews. A good outcome was defined as the mRS score of two or less, and a poor outcome was defined as the mRS score of three or more. The data were entered into and analyzed by using the Statistical Package for the Social Sciences (SPSS) version 25. The two outcome categories were compared based on the variables described above, and the calculation of the *P* value (considered statistically significant when $P < 0.05$) using relevant statistical tests was done (χ^2 test/Fischer exact test for categorical variables and t test/Mann–Whitney test for continuous variables). After univariate analysis, binary logistic regression analysis was carried out to assess the association between predictor variables and the outcome of the patient keeping other variables constant. Ethical clearance to carry out the study was obtained from the Institutional Review Committee of our university [Reference Number: 514(6-11)E2/077/078]. All data used in this study are anonymized.

Results

The total number of patients with acute stroke admitted during the second wave of COVID-19 (May 2021 until November 2022) was 75. Eleven patients were excluded as the patients could not be traced during the follow-up. The mean age of the patients was 60.25 ± 15.31 years. Four patients died (mRS = 6). Only seven patients presented to the ER of our hospital within 4.5 h duration. Mechanical thrombectomy and thrombolysis were not undertaken in any of the patients. The details of the study characteristics are shown in Table 1. Univariate analysis was done using relevant statistical tests and is shown in Table 2. A binary logistic regression analysis of the significant variables is shown in Table 3.

Discussion

The COVID-19 pandemic severely affected stroke care in most countries[2]. The number of code activations in stroke, admission rate, rate of reperfusion therapy, and time metrics in stroke care was all reduced compared to the pre-pandemic era[3,4]. There was a 42% global decline in stroke admission owing to the effect of the COVID-19 pandemic[3]. The total number of stroke patients in our center during the study duration of 7 months was 64, whereas it was found to be 343 in a study conducted for 12 months in the pre-pandemic era[12]. This may be due to the growing fear among the general public regarding the acquisition of COVID-19 during hospital stays. Recent surveys conducted in UK and France support this statement[13]. The current pandemic has affected the time for acute treatment. It has also caused the limited availability of rehabilitation services. Thus, this study was conducted to analyze the patterns of stroke, the causes and types of delay in the treatment of stroke during the second wave of the COVID-19 pandemic, and the outcomes of different types of stroke after 3 months of onset.

The mean age of the patients in our study was 60.25 ± 15.31 years which is similar to the findings of Devkota *et al.*[14] (61.7 ± 14.9) and Maskey *et al.*[15] (65.98 ± 10.69). The

Table 1

Detailed study characteristics showing frequency(percentage) and mean ± SD ($n = 64$).

	All ($n = 64$)
Age	60.25 ± 15.31
Sex, *n* (%)	
Male	37 (57.8)
Female	27 (42.2)
Address, *n* (%)	
Inside valley	18 (28.1)
Outside valley	46 (71.9)
Stroke type, *n* (%)	
LVO	31 (48.4)
Lacunar	13 (20.3)
Hypertensive hemorrhagic	6 (9.4)
Non-hypertensive hemorrhagic	1 (1.6)
Embolic	10 (15.6)
CVT	3 (4.7)
Onset, *n* (%)	
Witnessed	46 (71.9)
Unwitnessed	18 (28.1)
Time to ER, median (range)	24 (791.50)
Pandemic affected time to ER arrival, *n* (%)	
Yes	18 (28.1)
No	46 (71.9)
Reasons for delay ($n = 18$), *n* (%)	
Delay finding a vehicle	9 (50.0)
Delay arranging family members	2 (11.1)
Delay arranging finances	4 (22.2)
Bed unavailability	3 (16.7)
COVID-19 status, *n* (%)	
Positive	3 (4.7)
Negative	59 (92.2)
Not examined	2 (3.1)
NIHSS	8.51 ± 5.03
NIHSS stroke severity (NIHSS interval), *n* (%)	
Minor (1–4)	11 (17.2)
Moderate (5–15)	43 (67.2)
Moderate to severe (16–20)	6 (9.4)
No stroke symptoms (0)	4 (6.3)
Duration of hospital stay	8.79 ± 5.29
Progress during hospital stay, *n* (%)	
Improved	33 (51.6)
Static	31 (48.4)
Regular physiotherapy at physio-center ($n = 60$), *n* (%)	
Yes	32 (53.3)
No	28 (46.7)
Regular physiotherapy at home ($n = 60$), *n* (%)	
Yes	37 (61.7)
No	23 (38.3)
Speech and swallowing expert consulted ($n = 60$), *n* (%)	
Yes	2 (3.3)
No	58 (96.7)
Able to follow-up ($n = 60$), *n* (%)	
Yes	43 (71.7)
No	17 (28.3)
mRS, median (range)	3 (6)

CVT, cerebral venous thrombosis; ER, emergency room; LVO, large vessel occlusion; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale.

mean age of stroke is lower in low-middle income countries compared to high-income countries[16]. Our study showed male preponderance, which is in line with the study conducted in Nepal and with the global trend[15].

We found that most of the patients had LVO (48.40%) stroke followed by lacunar stroke (20.30%). Among the LVO patients, 67.70% had a poor outcome. A similar pre-pandemic study showed a lower frequency of LVO (17.90%) compared to lacunar stroke (46.40%)[9]. This might be because our center is a tertiary referral center, and those cases not managed in the periphery are being referred here, thus accounting for the increased frequency of more severe strokes like LVO. The worldwide trend shows the incidence of ischemic stroke is more than hemorrhagic stroke, but the ratio is found to be reversed in most of the hospital-based studies in Nepal[15,17]. But the incidence of hemorrhagic stroke was found to be just 11% in our case, similar to the universal findings. In one of the studies published by our team[12], the proportion of hemorrhagic stroke was around 26%, which is more than that obtained in this study. This might be because of the low number of patients enrolled in this study due to the ongoing COVID-19 pandemic. Actually, the proportion of hemorrhagic stroke in low or middle-income countries is higher than 20%, so the low percentage does not depict the true scenario in Nepal. Studies have shown that there is a decrease in the rate of ischemic and hemorrhagic stroke presentation by 25.3 and 27.6% compared to the pre-pandemic era[13].

A single-center study conducted in one of the hospitals of the capital city, where they studied the rate of mechanical thrombectomy, found that the rate decreased from 44.44 to 16.66% 3 months prior to the lockdown and after the lockdown. Similarly, the median duration of time to hospital arrival after symptom onset increased from 6 to 8 h[18]. The median time to ER arrival in our study was 24 h. Seven patients presented within 4.5 h duration to our hospital but none of them were subjected to thrombolysis treatment due to financial constraints and the unavailability of medications. Thrombectomy service was not available in our setup at that time. The cost of drugs used in thrombolysis outweighs the affordability of an average Nepali, considering the annual per capita gross domestic product of the country. Even without contraindications, many people are deprived of thrombolysis services due to financial concerns in Nepal[19]. A meta-analysis showed that the rates of intravenous thrombolysis and endovascular thrombectomy decreased by one-fourth and one-fifth during the pandemic[13]. Prehospital delay is one of the identified causes of low thrombolysis and thrombectomy rates. Owing to the safety precautions of the current COVID-19 pandemic, patients are less willing to come to the hospital[3]. Other factors like strict screening protocol, the risk of COVID to healthcare workers, and reluctance by the interventional team in the absence of the COVID-19 test are some of the other factors contributing to low rates of such interventions[8]. But the problem of delayed arrival existed even before the pandemic in low-income and middle-income countries (LMIC) due to limited stroke centers, poor management systems, financial constraints, poor transportation services including geographical challenges, poor health-seeking behavior of Nepalese people, and poor awareness regarding stroke symptoms[19]. Among the 18 cases that reported pandemics affecting their time to ER arrival, 50% of the cases had difficulty arranging vehicles owing to the strict COVID-19 protocol, such as the lockdown implemented by the country. Second, policies at the local level that require COVID-19 before entering certain cities have also resulted in arrival delays[18].

Patients with poor outcomes were in a greater number in our study. Recent data demonstrates that about 53% of stroke

Table 2

Comparison of study outcome with different study characteristics.

	Poor outcome, mRS ≥ 3 ($n = 35$)	Good outcome, mRS ≤ 2 ($n = 29$)	Row total	*P*
Age	60.77 ± 16.42	59.62 ± 14.12		0.67[a]
Sex, *n* (%)				
Male	17 (45.9)	20 (54.1)	37 (100.0)	0.10
Female	18 (66.7)	9 (33.3)	27 (100.0)	
Address, *n* (%)				
Inside valley	12 (66.7)	6 (33.3)	18 (100.0)	0.22
Outside valley	23 (50.0)	23 (50.0)	46 (100.0)	
Stroke type, *n* (%)				
LVO	21 (67.7)	10 (32.3)	31 (100.0)	**0.08**[b]
Lacunar	5 (38.5)	8 (61.5)	13 (100.0)	
Hypertensive hemorrhagic	4 (66.7)	2 (33.3)	6 (100.0)	
Non-hypertensive hemorrhagic	1 (100.0)	0 (0.0)	1 (100.0)	
Embolic	4 (40.0)	6 (60.0)	10 (100.0)	
CVT	0 (0.0)	3 (100.0)	3 (100.0)	
Onset, *n* (%)				
Witnessed	24 (52.2)	22 (47.8)	46 (100.0)	0.52
Unwitnessed	11 (61.1)	7 (38.9)	18 (100.0)	
Time to ER, median (range)	24(239.50)	24 (788)		0.16[a]
Pandemic affected time to ER arrival, *n* (%)				
Yes	11 (61.1)	7 (38.9)	18 (100.0)	0.52
No	24 (52.2)	22 (47.8)	46 (100.0)	
Reasons for the delay, *n* (%)				
Delay finding vehicle	7 (77.8)	2 (22.2)	9 (100.0)	
Delay arranging family members	0 (0.0)	2 (100.0)	2 (100.0)	
Delay arranging finances	2 (50.0)	2 (50.0)	4 (100.0)	
Bed unavailability	2 (66.7)	1 (33.3)	3 (100.0)	
COVID-19 status, *n* (%)				
Positive	3 (100.0)	0 (0.0)	3 (100.0)	0.31[b]
Negative	31 (52.5)	28 (47.5)	59 (100.0)	
Not examined	1 (50.0)	1 (50.0)	2 (100.0)	
NIHSS	11.08 ± 4.77	5.41 ± 3.32		**0.00**
NIHSS stroke severity, *n* (%)				
Minor	1 (9.1)	10 (90.9)	11 (100.0)	**0.00**[b]
Moderate	27 (62.8)	16 (37.2)	43 (100.0)	
Moderate to severe	6 (100.0)	0 (0.0)	6 (100.0)	
Normal	1 (25.0)	3 (75.0)	4 (100.0)	
Duration of hospital stay	10.80 ± 6.05	6.37 ± 2.73		**0.00**[a]
Progress during hospital stay, *n* (%)				
Improved	21 (63.6)	12 (36.4)	33 (100.0)	0.14
Static	14 (45.2)	17 (54.8)	31 (100.0)	
Regular physiotherapy at physio-center ($n = 60$), *n* (%)				
Yes	21 (65.6)	11 (34.4)	32 (100.0)	**0.02**
No	10 (35.7)	18 (64.3)	28 (100.0)	
Regular physiotherapy at home ($n = 60$), *n* (%)				
Yes	19 (51.4)	18 (48.6)	37 (100.0)	0.95
No	12 (52.2)	11 (47.8)	23 (100.0)	
Speech and swallowing expert consulted ($n = 60$), *n* (%)				
Yes	1 (50.0)	1 (50.0)	2 (100.0)	1.00
No	30 (51.7)	28 (48.3)	58 (100.0)	
Able to follow-up ($n = 60$), *n* (%)				
Yes	20 (46.5)	23 (53.5)	43 (100.0)	0.20
No	11 (64.7)	6 (35.3)	17 (100.0)	

[a]Mann–Whitney *U* test.

[b]Fischer's exact test.

CVT, cerebral venous thrombosis; ER, emergency room; LVO, large vessel occlusion; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale.

Bold value indicates outcome with significant *P* value.

Table 3

Binary logistic regression analysis ($P < 0.05$).

Variable	Odds ratio (OR)	OR with 95% CI	*P*
Sex	0.37	0.07–1.94	0.24
Time to the emergency room	1.00	0.99–1.01	0.50
NIHSS score	0.72	0.57–0.92	**0.01**
Duration of hospital stay	0.72	0.53–0.97	**0.03**
Regular physiotherapy at the physio-center	2.65	0.52–13.41	0.23
Progress during hospital	2.41	0.47–12.41	0.29
Improved			
Static			
Able to follow-up	0.20	0.02–1.62	0.13
Address	0.37	0.05–2.45	0.30
Inside valley			
Outside valley			

Bold value indicates outcome with significant *P* value

patients reported missed or delayed health center visits[20]. This may be due to delayed presentation and low awareness regarding subtle symptoms of stroke. Symptoms like subtle aphasia and paresis could be easily unnoticed by the patient, and with the strict social isolation of the COVID-19 pandemic, they lacked family/social support. Additionally, patients with indications of inpatient rehabilitation may refuse care due to fear of contracting the infection. The supplementary support system is an essential component for achieving independence for stroke patients, and such support in post-discharge cases includes family caregivers, friends and social support groups, recreational activities, and other community areas integrated into daily routines[21]. The COVID-19 pandemic halted various levels of participation in creating favorable home and community environments for those surviving strokes. There is also increased role and demand in the care a less supportive environment for caregivers leading to increased stress which ultimately results in compromised care for stroke patients.

The mean NIHSS score was 8.51 ± 5.03, which is similar to the findings of a study that showed a mean NIHSS score of 9.86 ± 6.12 and 9.99 ± 6.0 before and during the pandemic[8]. On multivariate analysis, we found that a higher baseline NIHSS score during hospitalization can be a predictor of poor stroke outcomes at 3 months of follow-ups [odds ratio (OR) = 0.72, $P < 0.05$]. The baseline NIHSS score was more in patients with poor outcomes. A study done in a similar setting[9] concluded that one unit increase in NIHSS score increases the odds of poor stroke outcome by 1.55 times. Similarly, a study by Jain *et al*.[22]. found that a higher NIHSS score was associated with more odds of worsening ambulatory function (OR = 3.28) and mortality (OR = 2.34). Thus, our findings reinforced the importance of the NIHSS score in predicting stroke outcomes.

The median duration of hospital stay was found to be another predictor of a good outcome at 3 months of follow-ups (OR = 0.72, $P < 0.05$). One unit increase in the median duration of hospital stay was associated with a 72% increase in the odds of having a poor outcome. As the severity of stroke increases, patients tend to have a more functional disability, and this could be one of the reasons behind delayed discharge from acute care. The median length of hospital stay was more for patients with moderate to severe stroke (NIHSS = 16–20) compared to the rest of the patients (10.5 vs. 7 days). Patients with longer hospital stays have a higher chance of acquiring nosocomial infections and infection, particularly pneumonia, which is associated with an increased risk of poor outcomes in stroke patients[23].

The establishment of effective stroke treatment centers where adequate stroke resources are secured and remain functional even in time of crisis is needed in many LMIC to improve stroke care. Centers should offer clinical visits virtually and reserve high-risk diagnostic methods only for emergencies during the time of crisis[24]. Similarly, a mass awareness program regarding early recognition and early medical care-seeking behavior is equally important. Tele stroke systems can be a good alternative to continue quality stroke care during the time of pandemic when health care is tested to its limit[25].

The limitations in our study are mostly due to the pandemic itself and the small sample size. As the cases of COVID-19-infected patients increased, the number of patients without COVID-19 infection admitted with stroke might have decreased. Some of the patients did not turn up at the specified time due to fear of contracting the virus. The telephone interview is not as reliable as an in-person evaluation. The hospital visit decreased as a result of transportation difficulties faced by the patient due to the pandemic. This is a single-center study, which explains the small size of the study, and it may not represent the scenarios in other hospitals in Nepal. A large-scale study involving a multi-center where such limitations can be mitigated can be carried out.

Conclusion

The COVID-19 pandemic has affected the overall care of stroke patients, including delays in admission, increased severity, and increased workload for decreased manpower in treatment of the ultimate outcome. The establishment of separate stroke-dedicated centers that can function even during the time of emergency, such as the COVID-19 pandemic, must be ensured. The factors that cause delayed transfer to hospital and treatment should be addressed, and mechanisms should be developed such that these factors do not hinder stroke care in the future.

Ethical approval

The study was approved by the ethics committees of the Institutional Review Committee of the Institute of Medicine, Tribhuvan University.

Consent

Written informed consent was obtained from the patient for the publication of this study.

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Author contribution

B.P.G. and S.G.: initiated the research, wrote the research proposal, conducted the research, did data entry and analysis, and wrote the manuscript; P.T. and A.P.: involved in the write-up of the methodology of the proposal and research work; S.G.:

contributed to the analysis of data; N.G. and A.S.: wrote and edited the manuscript; R.K., R.R., and R.O.: reviewed the manuscript. All the authors read and approved the final manuscript.

Conflicts of interest disclosure

No potential conflicts of interest relevant to this article exists.

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