

Case Series

Stroke in COVID-19 patients in Togo (2021)

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Abstract

Cases of stroke have been reported in COVID-19 patients. In sub-Saharan Africa where the SARS-CoV-2 pandemic has experienced some particularities, the link between stroke and COVID-19 is not well established. This study aims to describe the characteristics of strokes associated with COVID-19 in Togo during the SARS-CoV-2 pandemic.

A case series study including 36 patients confirmed positive for SARS-CoV-2 and suffering from stroke, hospitalised in the biggest Togolese centre for the care of patients with SARS-CoV-2 disease during the period from January to December 2021.

Of 1,043 hospitalised COVID-19 patients, 36 (3.4%) had a stroke (mean age = 59.0 ± 14 years, sex ratio = 1). Among them, 4 (11.1%) didn't have vascular risk factors. Hypertension was found in 86.1% of patients. The mean NIHSS was 9.7 ± 2.5. The types of strokes were mainly: ischemic stroke (80.6%) and intracerebral hemorrhages (16.7%). We recorded 12 deaths (33.3%). Impaired alertness (OR=7.60 [1.60-36.90]) and NIHSS on admission >15 (OR=16.40 [1.63-164.78]) associated with mortality ($p < 0.05$)

Strokes are relatively common in COVID-19 patients. The profile of these strokes is different from the one of the strokes outside the epidemic context by the greater frequency of ischemic stroke and higher mortality. COVID-19 appears to harm the frequency and outcome of strokes.

Introduction

The clinical presentation of SARS-CoV-2 infection (COVID-19), which constituted a global health emergency from 2020 to 2023, is highly polymorphous. The classic manifestations of the disease are those of respiratory viruses, ranging from mild upper respiratory tract infections to Acute Respiratory Distress Syndrome (ARDS) [1]. Neurological disorders, including stroke, have also been reported in patients infected with SARS-CoV-2 [2-7]. In these patients, the clinical profile and the outcome of strokes could be influenced by SARS-CoV-2 infection. The mechanisms of which are not fully

elucidated. In sub-Saharan Africa, where the SARS-CoV-2 pandemic has had certain specific features, the association between stroke and COVID-19 has not been documented. In Togo, stroke is a public health problem, with an incidence of 79 per 100,000 inhabitants in the capital, Lomé. Stroke is also the leading cause of hospitalisation, mortality and disability in neurology departments [8]. The first case of SARS-CoV-2 influenza was detected on 4 March 2020; by 30 December 2021, Togo had reported 30,163 cases of COVID-19 with 248 deaths [9]. This study aims to describe the possible clinical and outcome particularities of stroke in patients hospitalised for SARS-CoV-2 infection during the pandemic in Togo.



Methods

Type and period of the study

The present study was conducted at the Centre Hospitalier Régional-Lomé Commune (CHR-LC), the national health centre dedicated to caring for COVID-19 patients during the pandemic and located in Lomé. Patients were admitted to the centre when SARS-CoV-2 infection was confirmed by PCR (cobas® SARS-CoV-2), performed on nasal or oropharyngeal swabs in the national reference laboratory. This was a case series of 36 consecutive stroke patients with SARS-CoV-2 hospitalised at the CHR-LC between January 1 and December 31, 2021. All patients of either sex, aged 18 years or older, hospitalised during the study period at the CHR-LC for COVID-19 and presenting with a stroke according to WHO clinical criteria confirmed by cerebral imaging, which occurred less than two weeks before confirmation of SARS-CoV-2 infection or during hospitalisation after confirmation, were included.

Data collection and conduct of the study

Interviewing the patient and/or his family provided demographic information, antecedents and risk factors, the history of the disease and previous treatments. The physical examination was systematically carried out to look for focal neurological deficits, cognitive impairment and signs of damage to other systems, particularly the cardiorespiratory, renal and haematological systems. Complementary examinations were performed depending on the orientation of the diagnosis, in particular, brain CT scan or Magnetic Resonance Imaging (MRI), Electroencephalogram (EEG), common lab tests and Human Immunodeficiency Virus (HIV) serology. The COVID-19 PCR test samples were taken by doctors, nurses and laboratory technicians who had been trained beforehand.

Statistical analysis

Statistical analysis was carried out using Epi info software version 7.2.5 due to its accuracy. Frequencies or proportions described qualitative variables. The mean and standard deviation described quantitative variables. The statistical tests used were the Chi-2 test for qualitative variables and the Z test for continuous or discrete quantitative variables. To identify the factors associated with the occurrence of death, a bivariate analysis was used to study the association between the various factors and the occurrence of death. Once the factors had been selected through the bivariate analysis, a multivariate analysis followed: linear logistic regression to identify the prognostic factors for the occurrence of death. Odds Ratios (OR) were calculated, followed by their confidence intervals. Differences were considered statistically significant for $p < 0.05$.

Ethical considerations

Authorization was obtained from the director of CHR L-C. The anonymous nature of the survey was ensured. The data were used for scientific purposes only.

Results

Of 1,043 patients (542 males, 51.5%) hospitalised at the CHR-LC, 53 had a stroke, and 36 were enrolled in the study (17 were rejected for failure to meet the inclusion criteria) giving a frequency of 3.4%. The mean age was 59.0 ± 14 years (extremes: 20 and 86 years). The most common age group was 40-60 years. The sex ratio (male/female) was 1. Patients with primary level education and those in self-employment predominated, at 33.3% and 30.6% respectively. In 17 patients (47.2%), COVID-19 was minor to moderate and severe in 19 patients (52.8%) according to the WHO classification. Hypertension (86.1%) and diabetes (38.9%) were the most common cardiovascular risk factors. Patients with no identified cardiovascular (CV) risk factors accounted for 11.1% (Table 1).

Most (97.2%) of patients were hospitalised within more than 24 hours from stroke onset. Brain imaging was performed more than 24 hours after the onset of the neurological deficit in 35 patients (97.2%) and between 6 and 24 hours in the remaining patients. Stroke onset was abrupt in 94.4% of cases ($n = 34$). The patients were referred by various health centres in the country, and 77.8% of them ($n = 28$) had used medical transport to get to the CHR-LC. General examination on admission revealed hypertension in 66.7% of cases ($n = 24$) and hyperthermia in 41.0% of cases ($n = 15$). Neurological

Table 1: Socio-demographic characteristics and cardiovascular risk factors of SARS-CoV-2 positive stroke patients hospitalised at CHR-LC (Togo) in 2021 ($n = 36$).

Socio-demographic characteristics		Numbers (n)	Proportion (%) (%)
Gender			
	Female	18	50
Education level			
	Illiterate	4	11.1
	Primary	12	33.3
	Secondary	9	25.0
	University	11	30.6
Occupation			
	Civil Servant	8	22.2
	Liberal	11	30.6
	Retired	8	22.2
	Housewife/unemployed	9	25.0
Cardiovascular risk factor			
	No	4	11.1
	Yes	32	88.9
Hypertension		31	86.1
Diabetes type II		14	38.9
Dyslipidemia		12	33.3
Body mass index (kg/m2)			
	18,5 - 24,9	33	91.7
	≥ 25	3	8.3
Chronic alcoholism		3	8.3
Smoking		1	2.7



findings included motor deficit in 72.2% of cases ($n = 26$), with a mean NIHSS of 9.7 ± 2.5 , and impaired alertness in 36.1% of cases ($n = 13$). Cerebral infarctions accounted for 80.5% of strokes ($n = 19$) and involved the sylvian artery in 82.8% of cases. ASPECT and p-ASPECT scores were less than 7 in 26.7% of cases for the anterior circulation and 3.3% for the posterior circulation. Intracranial atherosclerosis and disease of the small cerebral vessel were the predominant aetiologies of cerebral infarction, each accounting for 37.9%. One case of emboligenic heart disease was found, accounting for 2.8%. Cerebral infarctions of undetermined cause accounted for 20.7%. Haemorrhagic strokes accounted for 16.7% ($n = 6$), including 5 cases of deep haematomas (83.3%) and one case of subarachnoid haemorrhage (16.7%). The ICH score was less than 3 in 66.7% of haemorrhagic strokes. Hypertension was the cause of deep haematomas and aneurysmal rupture of subarachnoid haemorrhage. There was one case of cerebral venous thrombosis involving the right transverse sinus (2.8%).

Complications during hospitalisation were essentially pneumopathy (52.8%), pressure ulcer (36.1%) and urinary tract infections (13.9%). The average length of hospitalisation was 10.4 ± 6.5 days, with extremes of 4 and 22 days. Twelve deaths were recorded, representing a mortality rate of 33.3%. The deaths included ten cases of cerebral infarction (27.8%) and two cases (5.5%) of haemorrhagic stroke, with mean times to death of 7.2 ± 6.1 days (extremes 1 and 22 days) and 7.0 ± 5.7 days (extremes 3 and 11 days) respectively. The bivariate analysis identified clinical factors associated with mortality ($p < 0.05$): impaired alertness (OR=2.18 [1.05-4.38]) and severe COVID-19 (OR=2.69 [1.06-7.06]) (Figure 1).

The mean age of patients with no CV risk factors was 41.7 ± 20 years (range: 20 and 57 years), all female; the mean age of patients with CV risk factors was 59.0 ± 52 years (range: 40 and 86 years), 40.0% female. Lacunar infarctions predominated (75.0%) and the mean NIHSS on admission was 7.5 ± 3.0 in patients without CV risk factors (Table 2).

Discussion

The incidence of stroke in COVID-19 patients at 3.4% is comparable to that reported by Bentabak, et al. [10] in Algeria

Table 2: Influence of cardiovascular risk factors in COVID-19 stroke patients hospitalised at Centre Hospitalier Regional Lomé-Commune (Togo) in 2021.

	Patients with CV risk factor (n = 32)	Patients without CV risk factor (n = 4)	P
Mean age (years)	59.0	41.7	< 0.01
Women (%)	40.0	100	< 0.01
Mean NIHSS	9.4	7.5	
Ischemic strokes (%)	76.7	100	< 0.01
Lacunar infarctus (%)	34.7	75.0	0.69
Mortality rate (%)	40.0	0.0	< 0.01

CV: Cardiovascular; NIHSS: National Institute of Health Stroke Score

in 2021. Among non-COVID-19 patients, Kumako, et al. [8] in Togo in 2023 reported an incidence of 0.08% in non-neurological settings. This relatively high incidence compared with the incidence of stroke in uninfected patients, could be directly linked to SARS-CoV-2, which is possibly one of the risk factors for stroke, or to a lack of patient follow-up during the pandemic. The mean age of patients in the study was 59.0 ± 14.0 years, comparable to that in the non-epidemic setting, which was 59.7 ± 14.1 years in Togo [8]. Hypertension (86.1%) and diabetes (38.9%) were pre-existing risk factors in the majority of patients. Similar results have been reported in the literature [11-16]. The same risk factors were incriminated in non-COVID-19 patients with stroke [8,17,18]. Half of the patients (52.8%) in the study had a severe WHO severity grade form of COVID-19, compared with 38.1% of severe cases in all patients hospitalised at the CHR-LC, confirming that stroke is a criterion of severity and poor prognosis. Cerebral infarctions predominated (80.5%), followed by haemorrhagic strokes (16.7%). In their studies, Nannoni, et al. [2] and Immovilli, et al. [11] reported 87.4% and 89.5% of cerebral infarctions and 11.6% and 10.5% haemorrhagic stroke respectively. In Togo, in hospital settings outside the epidemic, cerebral infarctions account for approximately 57% and haemorrhagic stroke for approximately 43% [8]. This suggests that SARS-COV-2 infection favours the occurrence of cerebral infarctions.

In our study, indeterminate causes of cerebral infarctions accounted for 20.7% and were mainly concerned with young subjects. Immovilli, et al. [11] reported, in order of frequency: undetermined cause (31.6%), embolismic heart disease (26.3%), and cerebral atherosclerosis (21.1%). According to studies by Yaghi, et al. [19] in the USA, patients suffering a stroke linked to COVID-19 were more likely to have an ischemic stroke subtype of undetermined cause in 66% of cases. Outside the epidemic context, Agbetou, et al. [17-18] reported that cerebral infarction of undetermined cause accounted for 19.0% in sub-Saharan Africa. This high frequency of indeterminate causes of cerebral infarctions could be linked to an unknown mechanism caused by COVID-19.

The neurological lesions observed in COVID-19 could be caused by two phenomena: direct neurotropism of SARS-CoV-2 and a hyperinflammatory state. Two pathophysiological hypotheses have been put forward to explain the virus pathway and neuronal damage [20,21]. The first is hematogenous dissemination of the virus. Once in systemic circulation, the

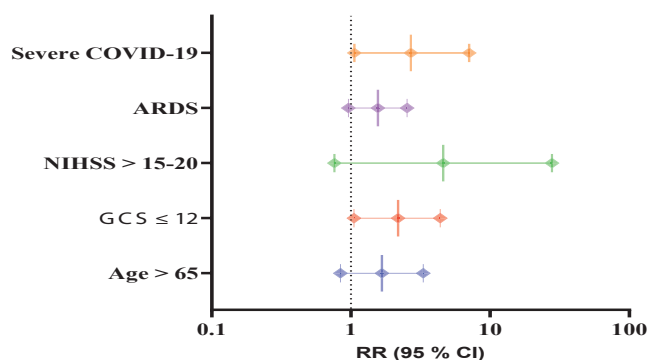


Figure 1: Clinical factors associated with mortality in COVID-19 stroke patients hospitalised at Centre Hospitalier Regional Lomé-Commune (Togo) in 2021. ARDS: Acute Respiratory Distress Syndrome; GCS: Glasgow Coma Scale; NIHSS: National Institute of Health Stroke Score; age (years).



virus could damage the blood-brain barrier, a phenomenon favoured by the presence of ACE2 receptors in the vascular endothelium. The second hypothesis is that the virus travels to the brain via the ethmoidal cribriform lamina, close to the bulb [22–24]. The second phenomenon explaining neurological impairment in COVID-19 is neuroinflammation. Direct viral invasion of endothelial cells causes inflammation or “endothelitis” and has been recognized as one of the substrates of thrombotic complications of COVID-19 [25].

We recorded 12 deaths in our series, representing a mortality rate of 33.3%. Our results are similar to those of Zieda, et al. [8]. In non-epidemic settings in Togo, early 30-day mortality rates vary between 27.5% and 25.6% [9] against 24.1% in sub-Saharan Africa [26]. The high mortality rate is justified by the occurrence of multiple complications, some directly related to the stroke and others to COVID-19, but also to a delay in initiating care due to failure to comply with barrier measures. In our series, pneumopathy, pressure ulcers and urinary tract infections dominated complications during hospitalisation. There have been very few studies on this subject in patients with SARS-CoV-2. It was difficult to determine whether distress syndrome was related to COVID-19 or to inhalation secondary to a swallowing disorder linked to stroke since it was difficult to investigate deglutition disorders. The high frequency of these complications is linked to several factors, including inadequate technical facilities, isolation of patients making follow-up difficult, and a lack of qualified human resources. In our study, the following independent risk factors for early in-hospital mortality were identified: impaired alertness and severe forms of COVID-19.

Conclusion

Stroke is relatively common in COVID-19 patients. The profile of these strokes differs from that of strokes outside the epidemic, with a higher frequency of cerebral infarction and high mortality. Studies are needed to determine the causal link between stroke and SARS-CoV-2 infection.

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