



Original Article

Pandemic impact on aneurysmal subarachnoid hemorrhage in Peru's high COVID-19 lethality setting: A public institutional experience

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ABSTRACT

Background: The COVID-19 pandemic in 2020 profoundly impacted healthcare worldwide, and Peru was particularly affected, experiencing the highest COVID-19 case fatality rate globally.

Methods: We conducted a retrospective comparative study of patients presenting with aneurysmal subarachnoid hemorrhage (SAH) at a public Peruvian national referral center specializing in cerebrovascular diseases. Two study periods were considered, one during the first wave of the COVID-19 pandemic and a second identical period in 2019. Variables included patient demographics, comorbidities, COVID-19 infection status, clinical presentation, treatment approaches, and hospital outcomes.

Results: We analyzed 114 patients with aneurysmal SAH, 65 (57.0%) treated in 2019 and 49 (43.0%) in 2020. The mean time from emergency admission to the day of definitive treatment during 2019 and 2020 was 2.72 and 1.93 days, respectively. Likewise, the mean time from symptom onset to the date of definitive treatment was 6.71 and 7.70 days, respectively. We identified significant associations between complications such as sepsis, respiratory failure, acute kidney failure, and hospital mortality. The proportion of fatalities was significantly higher in 2020 compared to 2019 (36.7% vs. 15.4%, respectively). Interestingly, there was no statistically significant association between COVID-19 infection status and mortality during the 2020 period.

Conclusion: Patients with aneurysmal SAH treated during the pandemic had a higher proportion of sepsis, respiratory failure, acute kidney failure, and mortality compared to the pre-pandemic period. Reallocating healthcare resources to prioritize COVID-19 patients may have inadvertently neglected or delayed care for patients with other emergency conditions, such as aneurysmal SAH. This highlights the importance of maintaining adequate care for non-infectious emergencies during a pandemic.

Keywords: COVID-19, Global neurosurgery, Latin America, Neurosurgical capacity, Subarachnoid hemorrhage

INTRODUCTION

Peru is one of the countries most affected by the COVID-19 pandemic. From January 2020 to March 2022, 3,517,260 cases and 210,672 deaths from this disease have been confirmed.

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According to the World Health Organization, Peru had the highest case fatality rate in the world due to this infection.^[27] The impact of the COVID-19 pandemic on patients with cerebrovascular diseases and subarachnoid hemorrhage (SAH) has been evaluated by multiple studies. The relationship between epidemiological aspects, clinical manifestations, and treatment implications has been well established as a major influencing force in the evolution and course of these patients.^[8,12] In our hospital, one of the major referral centers for cerebrovascular diseases in Peru, the evolution of patients with SAH has been negatively affected during the first wave of this pandemic, mainly due to the logistical limitations and collapse of our health system. This is despite the creation of new care protocols for patients with SAH in the context of the current pandemic,^[6,21] which is evidence of the weakness of our public healthcare system.

The main objective of this study is to evaluate the impact of the COVID-19 pandemic on the in-hospital clinical evolution of patients with aneurysmal SAH. Our specific goals are to identify the clinical-epidemiological characteristics of patients with aneurysmal SAH by comparing identical periods (March to October) in 2020 (pandemic context) and 2019 (pre-pandemic context) and to compare hospital stay, complications, functional status at discharge, and in-hospital mortality according to each study period.

MATERIALS AND METHODS

We conducted a retrospective and comparative study. It was performed in a single national referral center specializing in cerebrovascular diseases belonging to Peruvian social health insurance.

Our Institutional Review Board approved our study protocol in accordance with the Helsinki Declaration.

We divided the study into two study periods, one during the first wave of the COVID-19 pandemic (March to October 2020) and a second identical period in 2019. After a careful review of patient records, we included patients older than 18 years of age with aneurysmal SAH, corroborated by computer tomography (CT) angiography, and admitted during the study periods, regardless of the type of treatment performed. For the diagnosis of COVID-19 infection, polymerase chain reaction and chest CT were considered. Patients with incomplete data and those with SAH or intraparenchymal hematoma of different etiology were excluded from the study.

The following variables were assessed: provenance, age, gender, comorbidities (diabetes mellitus, high blood pressure, cancer, and smoking), COVID-19 infection status, clinical stratification at admission (Glasgow coma scale, Fisher scale, and WFNS score), initial symptoms, type of treatment (clipping, endovascular, or none), and hospital stay (including time in days from the onset of SAH symptoms to

admission, intervention, and discharge or death). During follow-up, we evaluated clinical complications (pneumonia, sepsis, surgical wound infection, venous thrombosis, electrolyte disorders, and acute respiratory or kidney failure), neurological complications (stroke, rebleeding, delayed cerebral ischemia-clinical vasospasm, and hydrocephalus), functional status at discharge (measured by the modified Rankin scale), and in-hospital mortality.

Statistical analysis

A descriptive analysis was performed using frequencies, percentages, and summary measures (mean, median, and standard deviation). The *t*-test was used to evaluate the differences between groups of patients in relation to a quantitative characteristic (previous assessment of normality). The Mann-Whitney test was used for the evaluation of quantitative variables with non-normal distribution. The Chi-square test was used to estimate associations between two qualitative variables, applying the Yates correction when appropriate (only when dichotomous variables were evaluated). When the assumption of having a minimum expected value of 5 was not fulfilled, and the variables were not dichotomous, the statistical association was considered not evaluable. A logistic regression method with 95% confidence intervals (CI) was applied to assess the risk of complications, poor functional status, and mortality related to the COVID-19 pandemic exposure. All data were analyzed using the statistical software Statistical Package for the Social Sciences version 25.0 (IBM Corp). A significant statistical association level was set at $P < 0.05$.

RESULTS

We analyzed records from 114 patients with aneurysmal SAH, 65 (57.0%) from the period March to October 2019 and 49 (43.0%) from the period March to October 2020 [Table 1].

The mean age of patients during the 2019 and 2020 periods was 57.6 (SD 13.53) and 58.63 (SD 15.28) years, respectively. Female sex predominated in both groups, 42 (64.6%) in 2019 and 39 (79.6%) in 2020. No significant association was found for epidemiological characteristics (gender, age, provenance, high blood pressure, diabetes mellitus, cancer, and smoking) regarding the study periods. There was also no significant statistical association between the clinical characteristics at admission and the study periods.

Of 114 patients included in the study, 45 (39%) underwent surgical clipping, 59 (51.9%) underwent endovascular therapy, and 10 (8.8%) did not receive any treatment [Table 1]. In the 2019 period, 65 patients were observed. Mortality during this time was 13.3% (4 of 30 patients) in the subgroup with surgical clipping, 3.3% (1 of 30 patients) in the endovascular subgroup, and 100% (5 patients) in those who did not receive any

treatment. During the 2020 period (49 patients), mortality was 33.3% (5 of 15 patients) in the subgroup with surgical clipping, 31.1% (9 of 29 patients) in the endovascular subgroup, and 80% (4 of 5 patients) in those who did not receive any treatment.

The mean time from emergency admission to the day of definitive treatment during 2019 and 2020 was 2.72 (SD 6.65) and 1.93 (SD 2.40) days, respectively. Likewise, the mean

time from symptom onset to the date of definitive treatment in both periods was 6.71 (SD 9.37) and 7.70 (SD 13.25) days, respectively. When evaluating these variables, we found no significant difference between the study periods [Table 2].

Length of hospital stay, complications, functional status at discharge, and hospital mortality for all cases by period are shown in Table 3. We identified a significant association

Table 1: Baseline and clinical characteristics of patients with aneurysmal SAH according to the study period.

	Total (n=114) n (%)	2019 (n=65) n (%)	2020 (n=49) n (%)	P-value*
Age at admission				
Mean [SD]	58.04 [14.26]	57.6 [13.53]	58.63 [15.28]	0.704
Gender				
Female	81 (71.1)	42 (64.6)	39 (79.6)	
Male	33 (28.9)	23 (35.4)	10 (20.4)	0.081
Provenance				
Other regions of Peru	27 (23.7)	19 (29.2)	8 (16.3)	
Foreigner	2 (1.8)	0 (0.0)	2 (4.1)	
Lima	85 (74.6)	46 (70.8)	39 (79.6)	NE†
Background				
High blood pressure	56 (49.1)	33 (50.8)	23 (46.9)	0.686
Diabetes mellitus	19 (16.7)	9 (13.8)	10 (20.4)	0.352
Cancer	5 (4.4)	3 (4.6)	2 (4.1)	0.499
Smoking	4 (3.5)	2 (3.1)	2 (4.1)	1.000
Clinical status				
Headache	111 (97.4)	63 (96.9)	48 (98.0)	1.000
Vomiting	84 (73.7)	48 (73.8)	36 (73.5)	1.000
Altered state of consciousness	76 (66.7)	43 (66.2)	33 (67.3)	0.894
Motor deficit	21 (18.4)	14 (21.5)	7 (14.3)	0.323
Fisher scale				
I	4 (3.5)	3 (4.6)	1 (2.0)	
II	13 (11.4)	8 (12.3)	5 (10.2)	
III	22 (19.3)	13 (20.0)	9 (18.4)	
IV	75 (65.8)	41 (63.1)	34 (69.4)	NE†
WFNS scale				
I	39 (34.2)	26 (40.0)	13 (26.5)	
II	47 (41.2)	25 (38.5)	22 (44.9)	
III	6 (5.3)	2 (3.1)	4 (8.2)	
IV	18 (15.8)	9 (13.8)	9 (18.4)	
V	4 (3.5)	3 (4.6)	1 (2.0)	NE†
Intervention				
Surgical clipping	45 (39.5)	30 (46.2)	15 (30.6)	
Endovascular	59 (51.8)	30 (46.2)	29 (59.1)	
None	10 (8.8)	5 (7.7)	5 (10.2)	NE†

SAH: Subarachnoid hemorrhage, SD: Standard deviation. *P-value according to Chi-square test, t-test, and Mann-Whitney test, †Non-dichotomous categorical variables considered not evaluable for statistical association

Table 2: Average time in days until definitive treatment according to the study period.

	Total (n=104) mean [SD]	2019 (n=60) mean [SD]	2020 (n=44) mean [SD]	P-value
Time from symptom onset to treatment	7.13 [11.18]	6.71 [9.37]	7.70 [13.25]	0.521
Time from hospital admission to treatment	2.38 [5.30]	2.72 [6.65]	1.93 [2.40]	0.858

SD: Standard deviation

Table 3: Hospital stay, complications, functional status, and mortality in patients with aneurysmal SAH according to the study period.

	Total (n=114) n (%)	2019 (n=65) n (%)	2020 (n=49) n (%)	P-value	OR (95% CI)
Average hospital stay					
Mean [SD]	22.6 [45.1]	24.7 [58.33]	19.9 [16.87]	0.576	-
Complications					
Pneumonia	51 (44.7)	26 (40.0)	25 (51.0)	0.241	-
Sepsis	22 (19.3)	6 (9.2)	16 (32.7)	0.002	4.77 (1.70–13.36)
Surgical wound infection	1 (0.9)	1 (1.5)	0 (0.0)	1.000	-
Venous thrombosis	2 (1.8)	2 (3.1)	0 (0.0)	0.604	-
Hydroelectrolytic disorder	28 (24.6)	15 (23.1)	13 (26.5)	0.672	-
Respiratory failure	40 (35.1)	16 (24.6)	24 (49.0)	0.007	2.94 (1.33–6.51)
Acute kidney failure	7 (6.1)	1 (1.5)	6 (12.2)	0.049	8.93 (1.04–76.82)
Brain ischemia	21 (18.4)	12 (18.5)	9 (18.4)	0.989	-
Delayed cerebral ischemia	42 (36.8)	20 (30.8)	22 (44.9)	0.122	-
Hydrocephalus	18 (15.8)	13 (20.0)	5 (10.2)	0.156	-
Functional outcome (mRS)					
Good (I–II)	47 (41.2)	28 (43.1)	19 (38.8)		
Poor (III–VI)	67 (58.8)	37 (56.9)	30 (61.2)	0.644	1.20 (0.56–2.54)
Hospital mortality	28 (24.6)	10 (15.4)	18 (36.7)	0.009	3.19 (1.31–7.77)

SAH: Subarachnoid hemorrhage, SD: Standard deviation, OR: Odds ratio, CI: Confidence interval, mRS: Modified Rankin scale. In bold and Italics, $P < 0.05$

between sepsis, respiratory failure, acute kidney failure, and hospital mortality with respect to the study periods. A higher proportion of patients with sepsis was observed in 2020 compared to the 2019 period, with 16 (32.7%) versus 6 (9.2%) cases, respectively ($P = 0.002$, odds ratio [OR]: 4.77, 95% CI: 1.70–13.36). Similarly, a significantly higher proportion of cases with respiratory failure was observed in the 2020 period, with 24 (49.0%) versus 16 (24.6%) cases ($P = 0.007$, OR: 2.94, 95% CI: 1.33–6.51). Furthermore, a higher proportion of patients with acute kidney failure was found in the 2020 period (12.2% vs. 1.5%) ($P = 0.04$, OR: 8.93, 95% CI: 1.04–76.82). We found no significant differences between the study periods when comparing the length of hospital stay and other neurological complications. No significant differences were found when comparing the functional status between both study periods ($P = 0.644$, OR: 1.2, 95% CI: 0.56–2.54).

Finally, we observed a significantly higher proportion of fatalities in 2020 than in the 2019 period (36.7% vs. 15.4%, respectively). The likelihood of death was approximately three times higher in patients in the 2020 period ($P = 0.009$, OR: 3.19, 95% CI: 1.31–7.77) [Table 3].

Regarding COVID-19 diagnosis, from March to October 2020, 14 (28.6%) cases of infection were reported in patients with aneurysmal SAH [Table 4]. During this period of the pandemic, no statistically significant association was observed between COVID-19 infection status and mortality ($P = 0.574$).

DISCUSSION

In our study, we observed a decrease in cases of aneurysmal SAH during the first wave of the COVID-19 pandemic

Table 4: Hospital mortality according to COVID-19 infection status.

COVID-19 infection	Hospital mortality			P-value*
	Yes	No	Total	
Negative	12	23	35	0.574
Positive	6	8	14	
Total	18	31	49	

*Chi-square test value: 0.316

(March–October 2020) compared to the 2019 period (49 vs. 65 cases). These findings are similar to those reported by several authors, such as Nguyen *et al.*,^[20] Nogueira *et al.*,^[22] and Bernat *et al.*,^[5] among others,^[4,13,15,26] who found a decline in admissions for acute ischemic and hemorrhagic cerebrovascular diseases during the 1st months of the pandemic in different countries worldwide. This decline was more evident in hospitals that received a high number of patients infected with COVID-19.^[4,13,28] These findings coincide with what we observed at our hospital, which during the 1st months of the pandemic was oversaturated by the high demand created by critical patients with this disease. Despite the possible association between COVID-19 infection and acute cerebrovascular complications,^[24] in addition to psychological stress and the risk of aneurysmal rupture,^[17] the admissions decline of patients with SAH is probably also related to the fact that those patients with moderate neurological symptoms did not seek medical care due to fear of infection,^[5] resulting in misdiagnosis or unknown deaths during lockdown. Patients with aneurysmal SAH who were not detected in time are part of the collateral damage left by the COVID-19 pandemic in our country.

For the management of ruptured aneurysms, we considered the clinical status of the patient and the anatomical characteristics of the aneurysm. The type of treatment performed, whether surgical or endovascular, depended on the logistics available on the patient's arrival at the hospital. During the 2020 period, we observed a decrease in the percentage of cases treated by surgical clipping and an increase in patients undergoing endovascular therapy [Table 1]. This finding was related to the shortage of emergency operating rooms, which were mostly adapted to treat patients with suspected or probable cases of COVID-19 infection. For most patients during the first wave of the COVID-19 pandemic (2020 period), it was more feasible to have an endovascular neurosurgery suite available for the management of ruptured aneurysms. It is important to note that this difference in surgical and endovascular treatment during the 2020 period did not have statistically significant effects in terms of mortality or patient outcomes.

Another interesting finding in our study corresponds to the time observed from the onset of symptoms to definitive treatment. In both study periods, the mean of this interval was between 6 and 8 days (slightly longer in the 2020 subgroup, without statistical significance), with a mean time from hospital admission to definitive treatment of about 2.5 days. A multicenter study conducted in Italy^[9] also observed a slight increase in time due to delays in diagnosis and hospitalization of patients with SAH during the pandemic; however, this did not influence the evolution or prognosis of patients. In a previous aneurysmal SAH study conducted in Peru,^[11] similar findings were reported in relation to the time interval from the onset of symptoms to emergency admission. In Peru, this delay can be explained in part by the logistical and transportation difficulties in transferring patients from different regions of Peru to our hospital, which is one of the few specialized centers in the country that treats patients with acute cerebrovascular disease requiring emergent neurosurgical treatment.

Regarding the evolution of the patients, it is important to remember that depending on the context, sepsis and septic shock can have a mortality rate of >40%. In addition, in patients with aneurysmal SAH, the risk of sepsis and systemic inflammatory response syndrome may be >50%.^[10] Our study showed a significantly higher proportion of sepsis, respiratory failure, acute kidney failure, and mortality during the first wave of the COVID-19 pandemic (2020 period) when compared to 2019. Despite some authors suggesting that COVID-19 infection could trigger SAH,^[3,24] Qureshi *et al.*,^[23] in a multicenter study of more than 280,000 patients, significantly found that COVID-19 infection is associated with a lower risk of aneurysmal SAH. However, the development of pneumonia, pulmonary embolism, acute kidney failure, respiratory failure, liver failure, and septic

shock was much higher in the group of patients with SAH and COVID-19 infection ($P < 0.0005$) when comparing them with patients without coronavirus infection. On the other hand, the same study found a higher rate of cerebral ischemia in patients with SAH and COVID-19.^[23] Our study did not observe statistically significant differences with respect to neurological complications such as cerebral ischemia, rebleeding, delayed cerebral ischemia, and hydrocephalus. We also found no significant differences regarding hospital stay or functional status of patients after discharge. Similarly, Kashefiolasl *et al.*^[15] found no statistically significant findings in relation to hospital stay, functional status, or neurological complications (vasospasm or hydrocephalus) when evaluating the impact of the COVID-19 pandemic on the evolution and management of patients with aneurysmal SAH. However, their study did not take into account variables such as sepsis, respiratory or renal failure, or multiorgan failure.

Ates *et al.*^[2] also found no association between COVID-19 infection and the occurrence of acute hemorrhagic cerebrovascular disease. However, they did find increased mortality in those patients with acute cerebrovascular disease and COVID-19 coinfection. Other studies^[1,23] have found that there is an increase in the severity of acute cerebrovascular disease in patients with simultaneous COVID-19 infection; however, they did not find increased mortality in their population analysis.

Qureshi *et al.*^[23] also observed a significant increase in deaths in patients with aneurysmal SAH and COVID-19 infection, which reached 31.4% ($P < 0.0001$). In our study, we did not find a statistically significant association between mortality and COVID-19 infection status in this subgroup of patients during 2020. This could be due to the small population recruited to perform the analysis since only 14 patients (28.6%) had COVID-19 infection, of which only six died. However, when comparing both periods, we were able to find evidence that the mortality of patients with aneurysmal SAH increased from 15.4% in the pre-pandemic period to 36.7% during the COVID-19 pandemic ($P < 0.005$). Due to these results, studies with a larger population would be necessary to perform an analysis with greater statistical power to determine the role of COVID-19 infection in the prognosis and mortality of the subgroup of patients with SAH during the pandemic. This is an important limitation to consider in our study.

The SVIN COVID-19 Global SAH Registry^[26], in a study published in 2022, evaluated the clinical characteristics, treatment, and evolution of patients with aneurysmal SAH during the period of the COVID-19 pandemic. A total of 187 hospitals in 49 countries were evaluated, comparing the results with a previous period without a pandemic. In the overall analysis, no significant variation was found in

hospital mortality when comparing both periods. However, a significant increase in mortality was found in the subgroup of hospitals with a high admission rate of patients with COVID-19 infection and aneurysmal SAH. Our hospital meets these last two characteristics since it is one of the hospitals that have seen the most patients with COVID-19 since the beginning of the pandemic. At the same time, it is one of the main centers of reference for aneurysmal SAH in our country.

Multiple studies have observed that the reorganization of resources for the medical care of patients with COVID-19 has triggered involuntary neglect of those patients without the infection who are in an emergency condition due to other causes.^[7,14,16,19,25] This situation, in which untimely or inadequate care occurs, results in increased morbidity and mortality in patients without COVID-19 in emergency departments.^[19] Therefore, the increased mortality and poor outcomes of the patients in our study could be related to causes different from COVID-19 infection in the context of the pandemic. Before the onset of the pandemic, we already had a small number of hospitals specialized in the management of acute cerebrovascular diseases, as well as a national shortage of healthcare personnel and intensive care unit (ICU) beds for this group of patients.^[18] With the outbreak of the COVID-19 pandemic in Peru, and despite the efforts to reorganize the limited health resources, our country has been one of the most affected internationally, with the highest case fatality rate worldwide related to COVID-19.^[27] Unfortunately, those patients with diseases other than coronavirus infection, who also required emergency medical management, have been adversely affected. This has been demonstrated in our results in the case of patients with aneurysmal SAH. For this reason, we believe that it is necessary to carry out additional studies with a larger population to show the critical points that can be improved in our milieu related to the care of patients with acute cerebrovascular disease in emergency services at a national level.

Finally, as lessons learned from this experience, we believe that it is essential to take action with regard to the following: First, we must always maintain strict surveillance for patients with SAH, especially after receiving the definitive surgical or endovascular treatment. Second, it is necessary to increase the number of ICU beds nationwide, ensuring the necessary equipment and supplies for the monitoring of neurosurgical patients. Third, to properly manage patients with SAH and other types of acute cerebrovascular emergencies, stroke units should be established and strengthened in the nation's major hospitals across all regions. Finally, an efficient referral system should be maintained for the timely transfer of patients in neurosurgical emergency conditions to centers with higher levels of complexity.

Limitations

Limitations of this study included the retrospective methodology and the size of the population that was considered. Due to the small number of people in the subgroup of patients with COVID-19 during the 2020 period, we were unable to perform a statistical analysis to assess the specific role of COVID-19 infection in the prognosis of patients with aneurysmal SAH. However, this study allowed us to assess the impact of the COVID-19 pandemic in the context of our healthcare system. More similar studies with a larger population would be necessary to perform an analysis with greater statistical power.

CONCLUSION

Peru has been significantly impacted by the COVID-19 pandemic, currently holding the unenviable distinction of having the highest case fatality rate across the globe. This has resulted in extensive challenges for Peru's healthcare system and economy, as well as for the wider population.

During the COVID-19 pandemic, there was a decrease in aneurysmal SAH admissions and a proportional decline in aneurysm surgical clipping for ruptured aneurysms. Moreover, there was an increase in the rate of coiling, suggesting a shift toward endovascular therapy during the pandemic.

We did not find a statistically significant association between COVID-19 infection and worse outcomes in patients with aneurysmal SAH in the subgroup evaluated during the pandemic. Nevertheless, the overall analysis found a significantly higher proportion of cases of sepsis, respiratory failure, acute kidney failure, and mortality in patients with aneurysmal SAH treated in the context of the COVID-19 pandemic when compared with the pre-pandemic period. We did not observe significant differences in terms of neurological complications, hospital stay, or functional status when comparing both study periods.

The reorganization of the health system's resources for the treatment of patients during a major pandemic can lead to the involuntary neglect of those patients who are in emergencies for other reasons. Attention must be focused on the importance of strict surveillance for SAH patients, increasing ICU beds nationwide, strengthening stroke units in major hospitals, and maintaining an efficient referral system for the timely transfer of neurosurgical emergency patients.

Ethical approval

The author(s) declare that they have taken the ethical approval from IRB, N° 42-IETSI-ESSALUD-2020, Research Ethics Committee Specific to COVID-19.

Declaration of patient consent

Patients' consent not required as patients' identities were not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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