Neurology Asia 2022; 27(3) : 599 – 607

Hospital admissions of spontaneous subarachnoid hemorrhage during the COVID-19 pandemic: Southeastern Turkey experience

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Abstract

Objective: This study aimed to determine if the coronavirus disease 2019 (COVID-19) pandemic had any impact on admission patterns for subarachnoid hemorrhage (SAH) during 1st and 2nd waves and in-between in a tertiary institution in southeastern Turkey. *Methods:* Three periods were determined during the pandemic: First and second peaks (April 1-May 1, 2020 and November 18-December 18, 2020, respectively) and the slowdown period (July 5-August 4, 2020) where the daily new cases hit its lowest. We retrospectively collected data of the patients with SAH who were admitted to our institution within these periods during 2020 (the pandemic) and 2019 (the year before the pandemic). Demographic data, time between symptom onset and admission, Glasgow Coma Scale (GCS), Fisher score, World Federation of Neurosurgical Societies (WFNS), presence of intracerebral hemorrhage, intraventricular hemorrhage, hydrocephalus, type of SAH (aneurysmal vs non-aneurysmal) were recorded and compared between the pandemic and pre-pandemic periods. *Results:* The number of admissions in first peak, slowdown, and second peak during the pandemic was 11, 15, and 17, respectively. They did not differ significantly from corresponding periods in 2019 (17, 7, and 10, respectively) (all P>0.05). The mean time from onset to admission to hospital was similar between pandemic and 2019 (ranging between 0.40-2.00 days in 2020 compared to ranging between 1.12-2.29 days in 2019). The rate of cases with worse neurological condition on admission turned out to be lower during the first peak of the pandemic compared to previous year (9.1% vs 29.4%, P=0.029), but showed no difference in the remaining two periods. The incidence of accompanying pathologies (intracerebral hemorrhage, intraventricular hemorrhage, and hydrocephalus) was also similar between the periods in 2020 and their counterparts in 2019. Rate of non-aneurysmal cases ranged between 11.1%-45.5% in 2020 compared to 10.0%-57.1% in 2019 (all P>0.05).
Conclusion: The study showed that hospital admission patterns for SAH was not affected by COVID-19 pandemic in the southeastern Turkey, unlike other reports. This may be due to different behavioral characteristics of the study population and capability of health care system to cope with high number of patient admissions.

Keywords: COVID-19, subarachnoid hemorrhage, pandemic, admission, pattern, Turkey

INTRODUCTION

During the coronavirus disease 2019 (COVID-19) pandemic, some papers reported changes in admission demographics of patients for serious neurological conditions compared to pre-pandemic era.[1] These changes were attributed to several factors such as dedication of health resources to the control and treatment of the pandemic, fear of getting infected, and delayed admissions.[2-4]

The published studies were heterogenous as some included only stroke patients, some included nontraumatic subarachnoid hemorrhages (SAH) (aneurysmal only or all), some included intracranial hemorrhages and some included all together. Though hemorrhagic stroke, intracerebral hemorrhage and SAH are subtypes of intracranial hemorrhages, they are distinct pathologies and have different pathophysiologies, presentations, and prognosis. Thus, evaluating all of them under a single group would be inconclusive. And as stated in a recently published meta-analysis on stroke and SAH, the available data is too little to reach conclusions regarding SAH admissions during the pandemic.[5]

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Date of Submission: 31 January 2022; Date of Acceptance: 29 March 2022

https://doi.org/10.54029/2022ydf

Papers focused on admission patterns of SAH cases during COVID-19 pandemic are scarce and mostly of European and United States origin.[4,6-11] To the best of our knowledge, apart from a multinational study, there is no study that reports admission patterns of SAH in Middle East countries which has different health care structuring and social behavioural pattern.[7]

In this study, we aimed to evaluate if COVID-19 had an impact on admission patterns of patients with SAH at various time points during the 1st year of COVID-19 pandemic as observed in a single institution located in southeastern part of Turkey.

METHODS

The study was approved by institutional ethics committee (Dicle University Medical Faculty Ethics Committee for Noninterventional Studies, Date: 27.05.2021, No: 283). Since the study was based on retrospective analysis of patient records, patient consent was not required and not sought after.

We retrospectively reviewed adult patient records that were admitted or referred to the study institution and diagnosed with spontaneous SAH at three separate periods within the first year of the pandemic. The periods were: Period 1: the interval where the daily new cases were highest during the first wave, Period 2: the slowdown period where the daily new cases were lowest in between two waves, and Period 3: the interval where the daily new cases were highest during the second wave. The exact dates for these periods were determined based on official daily new COVID-19 cases nationwide declared by the Ministry of Health which all turned out to be in 2020.[12] Using the institutional database, control groups were established covering the same periods in 2019 and similar data were extracted. Patients younger than 18 years old and those with traumatic SAH were excluded from the study.

The institution where the study data was collected is a tertiary health center serving over 2 million people with a capacity of 4,200 outpatients per day and 2,500 surgeries per month.[13] Almost all patients with spontaneous SAH who in the close vicinity are referred to this institution by primary and secondary health centers, mostly within a few hours, and none later than 24 hours. Average number of surgeries for intracranial aneurysms (either with or without SAH) is approximately 80-100 annually.

From the institutional patient records, age, the interval between onset of symptoms and hospital admission (in days), neurological condition at admission (stratified according to Glasgow Coma Scale (GCS)) were recorded. Standard Fisher score, World Federation of Neurosurgical Societies (WFNS) grade, and presence of accompanying pathologies (intracerebral hemorrhage, intraventricular hemorrhage, hydrocephalus) were determined by authors using patient records and evaluating imaging studies. Origin of SAH (aneurysmal vs non-aneurysmal) was also recorded for each case based on computed tomography angiography and/or digital substraction angiography reports which were also double-checked by authors for any error.

The data for selected periods during the pandemic were compared with the corresponding periods during 2019.

Statistical Analysis

The statistical analysis was performed using SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA). The continuous variables were analyzed by the Shapiro-Wilk test for normality. The normally distributed data were compared using student t-test between the groups, whereas nonnormally distributed data were compared with the Mann-Whitney U test. Continuous variables were reported as means with standard deviation. Intergroup comparisons for categorical data were made using the chi-square test. Categorical variables were reported as percentages and count. To compare the number of admissions between the pre-pandemic and pandemic periods, Poisson Means test was used. $P<0.05$ was considered statistically significant.

RESULTS

Based on Ministry of Health data, the day with the highest new COVID-19 cases per day (5138 new cases) nationwide was April 11, 2020 during the first wave. We determined the first interval as the period between April 1- May 1 (Period 1), where the new cases per day were highest (108,861 new cases in this 31-day interval in 2020). The second interval was the period where the daily new cases hit their lowest. The lowest number of daily new cases was on July 22, 2020 with 902 new cases. The period was determined as between July 5-August 4 (Period 2) (30,324 new cases in this 31-day interval in 2020). The second wave was entered towards the end of the year with

7381 new cases on November 24, 2020. The period during the second wave was determined as November 18-December 18 interval (Period 3) (182,308 new cases in this 31-day interval in 2020). The database search yielded a total of 25 and 34 patients in the pandemic (2020) and pre-pandemic (2019) periods, respectively.

The age parameter in all periods and WFNS in Period 2 group showed normal distribution and age variable was evaluated by student t-test. Time to admission, GCS, WFNS, and Fisher scores were evaluated using the Mann-Whitney U test. Gender, aneurysmal/non-aneurysmal origin, and accompanying pathologies were evaluated by chi-square test.

Period 1: When the first pandemic peak in 2020 was compared with the year before, we found that the number of admissions was dropped by 35.3% compared to the previous year (11 vs 17, respectively). But Poisson Means test turned out with a P value of 0.34 (Table 1).

There was no significant difference between mean age and gender distribution. Also, there was no significant delay in time to admission during 2020 compared to 2019. There was no significant change in the aneurysmal/non-aneurysmal SAH ratio, however we omitted 2 patients from the analysis since no diagnostic studies were performed on them. When clinical parameters at the time of admission were analyzed we found that both years were similar regarding WFNS grade, Fisher score, as well as incidence of intracerebral hemorrhage, intraventricular hemorrhage, and hydrocephalus at the time of admission. We found that patients were in good neurological condition based on GCS scores on admission during the pandemic ($P<0.05$). However, when absolute GCS scores were taken into account rather than stratified categories, there was no statistical difference ($P>0.05$). The data regarding Period 1 in 2019 and 2020 were summarized in Table 2.

Period 2: The number of admissions during this period was similar in 2019 and 2020 (Table 1). Mean age and gender distribution showed no significant variation between the two years. The mean time to admission was shorter during the pandemic, but the difference was not significant. Neurological status, WFNS, and Fisher scores also were not different in the pandemic (2020) compared to the pre-pandemic (2019) period. Excluding hydrocephalus which wasn't present in any patient of this period, intracerebral and intraventricular hemorrhage were both observed at a similar rate. The aneurysmal SAH ratio was also similar between the two periods. The data is expressed in Table 3.

Period 3: The number of admissions during the second peak of the pandemic (2020) was similar to the same period of the previous year (Table 1). Similar to the other periods, there were no significant differences between the pandemic and non-pandemic periods regarding mean age and gender distribution. The patients were admitted to the hospital within a similar time frame after the onset of symptoms during both periods. The patients in both periods had similar neurological status, WFNS and Fisher scores at the time of admission. Intracerebral and intraventricular hemorrhages, as well as hydrocephalus, were observed at similar rates in the same period of both years. The data is summarized in Table 4.

A post-hoc Poisson means test to assess changes across three study periods in each year revealed non-significant results.

Table 1: Number of SAH admissions during the same periods of the years 2019 and 2020

Periods	Years	n	95% CI	P
Period 1				0.34
	2020	11	5.5 – 19.7	
	2019	17	9.9 – 27.2	
Period 2				0.77
	2020	5	1.6 – 11.7	
	2019	7	2.8 – 14.4	
Period 3				0.63
	2020	7	2.8 – 14.4	
	2019	10	4.8 – 18.4	

n: number of cases, CI: confidence interval, P: P value for Poisson Means test

Table 2: April 1-May 1 interval (Period 1) in 2019 and 2020

		2019 (n=17)	2020 (n=11)	P
Age (years)		50.94 ± 15.23	55.73 ± 10.62	0.373
Gender (Female)		10 (58.8%)	7 (63.6%)	0.799
Time from onset to hospital admission (days)		1.12 ± 2.12	1.36 ± 1.69	0.458
GCS				0.029*
	3-8	5 (29.4%)	1 (9.1%)	
	9-13	9 (52.9%)	3 (27.3%)	
	14-15	3 (17.6%)	7 (63.6%)	
WFNS				0.147
	1	3 (17.6%)	6 (54.5%)	
	2	6 (35.3%)	2 (18.2%)	
	3	1 (5.9%)	0 (0.0%)	
	4	5 (29.4%)	2 (18.2%)	
	5	2 (11.8%)	1 (9.1%)	
Fisher				0.643
	1	2 (11.8%)	0 (0.0%)	
	2	4 (23.5%)	2 (18.2%)	
	3	2 (11.8%)	3 (27.3%)	
	4	9 (52.9%)	6 (54.5%)	
ICH		6 (35.3%)	1 (9.1%)	0.118
IVH		7 (41.2%)	5 (45.5%)	0.823
Hydrocephalus		4 (23.5%)	4 (36.4%)	0.463
Nonaneurysmal		3 (17.6%)	5 (45.5%)	0.165

GCS: Glasgow Coma Scale, WFNS: World Federation of Neurosurgical Societies, ICH: intracranial hemorrhage, IVH: intraventricular hemorrhage

DISCUSSION

In this study, there was no delay in admissions during pandemic compared to pre-pandemic in any timeframe. In the 1st period, the number of spontaneous SAH admissions in 2020 was 35.3% lower than those in pre-pandemic, but neurological status of those patients was significantly better in 2020 compared to 2019. In 2nd and 3rd periods, time to admission and neurological status of the patients did not differ significantly between pandemic and pre-pandemic. The accompanying pathologies and incidence of non-aneurysmal SAH showed no difference between the pandemic and pre-pandemic in any period.

Admission numbers

Some authors have reported a reduced number of hospital admissions for non-COVID-19 emergent diseases (ie. myocardial infarction, ischemic stroke, nontraumatic subarachnoid hemorrhage) during the COVID-19 pandemic.[9,14-17] Both Tavaneai *et al*. and Siegler *et al*. found that this reduction in stroke admissions was mostly in the mild cases and suggested that mild cases might have avoided seeking healthcare.[14,15] Bhambhvani *et al*. and Bernat *et al*. reported similar trends for SAH cases in United States and France, respectively.[3,9] Bernat proposed several explanations such as fear of getting infected, misdiagnosis as a result of overload on health systems, reduced stress levels and unknown deaths among quarantined people.[3] On the other hand, in another study from France, Aboukais *et al*. stated that the number of admissions for aneurysmal SAH was similar in 2019 and 2020.[4] Similarly, De Bonis *et al*. reported no reduction in admission numbers for hemorrhagic cerebrovascular diseases with vascular origin in 2020 compared to previous two years.[8] More interestingly, Theofanopoulos *et al*. reported an increased admissions for SAH during the pandemic.[10] They attributed this increase to increased stress which can lead to SAH by elevating blood pressure, possible relocation of the people in the area due to lockdown, and less misdiagnosis caused by less pressure on health

Table 3: July 5-August 4 interval (Period 2) in 2019 and 2020

		2019 (n=7)	2020 (n=5)	P
Age (years)		61.43 ± 20.85	44.80 ± 8.23	0.125
Gender (Female)		5 (71.4%)	3 (60.0%)	0.679
Time from onset to hospital admission (days)		2.29 ± 5.619	0.40 ± 0.894	0.876
GCS				1.000
	3-8	1 (14.3%)	2 (40.0%)	
	9-13	3 (42.8%)	0 (0.0%)	
	14-15	3 (42.8%)	3 (60.0%)	
WFNS				0.838
	1	3 (42.8%)	2 (40.0%)	
	2	1 (14.3%)	1 (20.0%)	
	3	0 (0.0%)	0 (0.0%)	
	4	2 (28.6%)	0 (0.0%)	
	5	1 (14.3%)	2 (40.0%)	
Fisher				0.432
	1	1 (14.3%)	0 (0.0%)	
	2	1 (14.3%)	0 (0.0%)	
	3	2 (28.6%)	2 (40.0%)	
	4	3 (42.8%)	3 (60.0%)	
ICH		2 (28.6%)	2 (40.0%)	0.679
IVH		3 (42.8%)	3 (60.0%)	0.558
Hydrocephalus		0 (0.0%)	0 (0.0%)	-
Nonaneurysmal		4 (57.1%)	1 (20.0%)	0.198

GCS: Glasgow Coma Scale, WFNS: World Federation of Neurosurgical Societies, ICH: intracranial hemorrhage, IVH: intraventricular hemorrhage

care system as a result of strict lockdown.[10] A multinational study covering 6 continents and 37 countries also reported a decreased number of SAH admissions during the first wave of the pandemic.[7] But when looked into the data regionwise, authors stated that decreases were observed in Asia, North and South America, and Europe, but not in Australia and Africa confirming the heterogenity of the situation across countries.[7] Considering varying results from different countries, we think that both the differences in health care structuring and people's behaviours play role in this discriminancy.

In this study, admission numbers did not differ in 2nd and 3rd periods compared to previous year. Though admission numbers was 35% lower in the 1st period compared to previous year, the difference was not significant. Moreover, the significantly higher rate of patients with good neurological status in this period contradicts the idea that mild cases have avoided admitting to health centers. Similarly, admission numbers during 3rd period were not different from the previous year despite an even higher number of daily new cases compared to 1st period. There are possible reasons behind these findings: 1. The pandemic did not affect people's behavior and did not stop them admitting to health facilities. 2. Despite fear of getting infected, people just couldn't neglect the severe symptoms of SAH and eventually sought medical healthcare. 3. As Lee *et al*. stated, psychological stress is a robust predictor of aneurysm rupture and those additional SAHs secondary to increased anxiety might have balanced out those who did not seek healthcare resulting in similar numbers of admissions.[18] 4- The daily admission numbers to emergency departments in Turkey vary between one to several hundreds in normal routine practice which shows people's tendency to seek healthcare relatively easily. Unlike Europe or United States, healtcare workers are used to cope with such a high number of patients and thus, overload caused by the pandemic didn't hamper their abilities to

Table 4: November 18-December 18 interval (Period 3) in 2019 and 2020

		2019 (n=10)	2020 (n=9)	P
Age (years)		38.90 ± 18.85	49.89 ± 12.92	0.161
Gender (Female)		6 (60.0%)	4 (44.4%)	0.498
Time from onset to hospital admission (days)		1.20 ± 1.87	2.00 ± 4.90	0.968
GCS				0.278
	3-8	1 (10.0%)	1 (11.1%)	
	9-13	4 (40.0%)	1 (11.1%)	
	14-15	5 (50.0%)	7 (77.7%)	
WFNS				0.095
	1	3 (30.0%)	7 (77.7%)	
	2	4 (40.0%)	1 (11.1%)	
	3	0 (0.0%)	0 (0.0%)	
	4	3 (30.0%)	1 (11.1%)	
	5	0 (0.0%)	0 (0.0%)	
Fisher				0.156
	1	0 (0.0%)	2 (22,2%)	
	2	1 (10.0%)	2 (22,2%)	
	3	5 (50.0%)	3 (33,3%)	
	4	4 (40.0%)	2 (22,2%)	
ICH		1 (10.0%)	1 (11.1%)	0.937
IVH		4 (40.0%)	2 (22,2%)	0.405
Hydrocephalus		2 (20.0%)	0 (0.0%)	0.156
Nonaneurysmal		1 (10.0%)	1 (11.1%)	0.937

GCS: Glasgow Coma Scale, WFNS: World Federation of Neurosurgical Societies, ICH: intracranial hemorrhage, IVH: intraventricular hemorrhage

correctly diagnose a SAH case. On the other hand, the significantly higher number of patients with good neurological status in the 1st period might be due to headache being one of the symptoms of COVID-19 infection which led people to admit to health centers to rule out a possible infection even for a mild headache.

Time to admission

Compared to studies that focused on admission numbers, very few studies have focused on admission delays. Fiorindi *et al*. and Aboukais et al found a significant diagnostic delay during the pandemic compared to pre-pandemic.[4,6] Fiorindi *et al*. attributed this to overcrowding in health centers and patients' fear of hospitalization.[6] According to Aboukais *et al*., the patients, especially those with mild symptoms, might have avoided admission to the hospital due to potential encounters with COVID-19 individuals.[4] Also, the oversaturation of the health centers might have discouraged them to seek healthcare.[4] People might have followed the recommendations of staying at home and social distancing, thus avoiding seeking healthcare for mild complaints.[4] And some might have simply attributed their headache to COVID-19 infection rather than a neurological disorder.[4] These all might have played role in delayed admissions. However, whether these reasons can keep patients waiting until their neurological conditions worsen significantly is not clear. In this study, there was no delay in admissions in none of the periods compared to the previous year. We think that this resulted from patients' attitude towards the pandemic, their habit of using healthcare systems, and the capacity of the health systems to deal with an overload of patients that we discussed in the previous section.

Neurological status at admission

Similar to delayed admissions, very few studies reported SAH patients' neurological status at admission during the pandemic. Aboukais et al found that the frequencies of intracerebral

hemorrhage, and hydrocephalus were higher in 2020 compared to 2019.[4] It has been reported that intracerebral hemorrhage frequency was around 21% in a large series of aneurysmal SAH and they had a poorer neurological condition on admission as well as worse outcome.[19] This may be due to rebleeding of an aneurysm as a result of delayed admission and management.[20] Aboukais *et al* also stated that aneurysmal SAH cases in worse condition have increased to 58% in the pandemic compared to 21% the year before.[4] They attributed this to delayed admission of patients as similar findings were reported by Goertz *et al*.[4,21] The higher incidence of intracerebral hemorrhage might have also played role in poorer neurological conditions seen in the admissions during pandemic.[4] On the contrary, in Fiorindi *et al*.'s study, despite a significant diagnostic delay, there was no significant difference in WFNS and Fisher scores at admission between pandemic and pre-pandemic era.[6] This discriminancy between two studies might have arised from amount of delay. In Aboukais *et al*.'s study difference between mean time-to-admissions was close to 2 days while it was less than half a day in Fiorindi *et al*.'s study.[4,6] Though the difference was significant in both studies between the pandemic and pre-pandemic, 12 hours of delay might not have impacted clinical picture whereas 2-day delay was sufficient enough for clinical picture to worsen.[4,6] There was no difference regarding intracerebral hemorrhage, intraventricular hemorrhage, or hydrocephalus between the pre-pandemic era and the pandemic era in this study. Since we did not found significantly delayed admissions during the pandemic period, this is an expected finding.

When looked at the three periods during the pandemic, the admission numbers of SAH patients showed a nonsignificant drop during Period 2. Neither in 2020 nor in 2019, there was a significant difference in admission numbers between any periods according to Poisson Means test.It can be speculated that the incidence of SAH might have increased as the pandemic intensified based on the reports regarding cerebrovascular events in patients with COVID-19.[22,23] Also, it has been suggested that COVID-19 infection may be a predisposing factor for SAH.[24] However, we do not think it is the case here since there was a similar trend in 2019 which suggests that there might be other factors behind our findings. The inhabitants of the region tend to travel to other parts of the country as seasonal workers which might have caused a decrease in population during 2nd period and so SAH cases. Also, if COVID-19's association with cerebrovascular events was valid in SAH, we would expect a higher incidence of non-aneurysmal SAH cases which we did not observe. Moreover none of the patients in these 3 periods have COVID-19 history.

The limitations of this study is that first, that it is retrospective in nature and findings are based on pre-recorded data. Though the institution where the study was held serves a population above 2 million, it's still a single center study. Additionally, the study have small sample size, but considering annual incidence of aneurymal SAH cases, our sample size is within expected range for the study period.[25] Also, though vasospasm on admission is a poor prognostic factor, due to institutional technical and staff limitations, reliable data from imaging studies could not be obtained.[26] However, since the main investigation point of this study was the effect of the pandemic on the admission numbers and status, the development of vasospasm after the admission didn't affect that aspect. Also, as admission patterns vary across different countries, it may vary regionally as well. Though health care structuring is uniform throughout the country, there are cultural and behavioral differences between various regions. For example, while western part of Turkey resembles Europe culturally, eastern parts of the country is more close to Middle East culture. Thus, these findings can not be generalized to whole country.

The study is important, because it depicts a picture of COVID-19 pandemic's effect on spontaneous SAH admissions in a region where there is a lack of respective data. Second, almost all studies focused on the period of first wave of the pandemic. This study evalutes not only the 1st wave, but also 2nd wave and slowdown period between the waves and individually compares them with respective control periods.

In conclusion, the effect of COVID-19 pandemic on admission numbers, time-to-admission and neurological status at admission is not uniform throughout the world and can show variation between countries. This variation may result from the country-dependent and population-specific factors. Considering southeastern Turkey, the study showed COVID-19 pandemic didn't affect admission numbers of SAH cases or caused any significant delay in admission. This finding might not be valid for other parts of the world and the awareness of healthcare professionals for SAH symptoms, especially the headache, should be re-established and proper and timely referral to neurosurgery departments must be maintained.

DISCLOSURE

Financial support: None

Conflict of interest: None

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