Spontaneous Intracerebral Hemorrhage: Profile of Patients Treated in the Stroke Unit of a Third Level Hospital

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Abstract

Introduction: Constituting around 15% of all strokes, intracerebral hemorrhage is the most devastating cerebrovascular event. Despite its impact, only a few regional studies analyze its characteristics separately.

Aim: Describe the characteristics of spontaneous intracerebral hemorrhage patients, treated at the Stroke Unit of a tertiary hospital of Costa Rica´s National Social Security Health System (CCSS).

Patients and Methods: By reviewing medical charts, a retrospective study and analysis of socio-demographic and clinical characteristics in well defined, arterial, spontaneous, and non-traumatic intracerebral hemorrhage patients, was performed.

Results: Clinical records of 74 patients were studied. Age average was 64.4 ± 12.6 years, events were identified predominantly in male patients and all patients presented at least one risk factor; being arterial hypertension the most prevalent. Etiology in 90.5% of the cases corresponds to small vessel disease, 81.0% of the events are consistent with deep intracerebral hemorrhage and 3 months modified Rankin Scale median was 3. The average hospital stay at the unit was one week, around one third of patients presented complications and 90-day mortality was 16.2%.

Conclusions: Despite the differences found attributable mainly to ethnic aspects and the nature of the analyzed population, the profile of these patients resembles what has been described elsewhere.

Keywords: Spontaneous Intracerebral Hemorrhage; Cerebrovascular Disease; Tertiary Referral Hospital; Stroke Unit; Patients Profile

Abbreviations

AMI: Acute Myocardial Infarction; AVM: Arteriovenous Malformations; CCSS: Costa Rica´s National Social Security Health System; CVD: Cerebrovascular Disease; DALYs: Disability-Adjusted Life Years; DM: Diabetes Mellitus; HSJD: San Juan de Dios Hospital; HT: Hypertension; ICH: Intracerebral Hemorrhage; IQR: Interquartile Range; LOS: Length of Hospital Stay; mRS: Modified Rankin Scale Score; mRS-3M: mRS Score at 3 Months; MV: Mechanical Ventilation; OR: Odds Ratio; PEG: Percutaneous Endoscopic Gastrostomy; SD: Standard Deviation; SU: Stroke Unit; SVD: Small Vessel Disease; UTI: Urinary Tract Infection

Introduction

Worldwide, cerebrovascular disease (CVD) is considered: the second leading cause of death, one of the main causes of disability and a fundamental source of disability-adjusted life years (DALYs) lost [1-3]. More than 20 million strokes occur annually, constituting a global public health concern that strongly impacts developing countries [4]. By 2013, 75.2% of all deaths and 81.0% of all DALYs related to CVD, occurred in developing countries [5,6].

Intracerebral hemorrhage (ICH) is the most devastating and disabling condition within CVD [7,8]. The clinical presentation is usually a sudden onset of a focal neurological deficit, caused by the non-traumatic rupture of an intracerebral vessel that generates extravasation [6,9,10] and compression of the cerebral parenchyma. The most important cause of spontaneous ICH, constituting between 70 and 80% of cases, is small vessel disease type-1 or arteriolosclerosis, which is related to age and vascular risk factors, mainly hypertension (HT) [11-13]. The condition can also derive from the presence of weakened blood vessels secondary to aneurysms and/or arteriovenous malformations (AVM) [14].

Considering the pathogenesis for CVD, and even though ICH is less frequent, constituting between 15 and 20% of all acute strokes [15] it has the highest mortality rate [16], which is estimated to be between 40% and 60% [9,17]. Half of all the deaths caused by this disease occur during the first 48 hours of the event, and can reach a 55% mortality rate during the first month. Bearing that in mind, ICH is one of the leading causes of severe disability worldwide [18-21].

Neurological manifestations experienced by the patients, will depend on the anatomical location of the hemorrhage; ataxia is the initial deficit observed in a cerebellar hemorrhage, while weakness can be the initial symptom in basal ganglia hemorrhage. However, most ICH patients present acute signs and symptoms during waking hours, when the patient is active, including: a sudden onset headache, vomiting, loss of consciousness and a severe increase in blood pressure [22-24].

Age is considered the main risk factor for acute hemorrhagic cerebrovascular disease, as a result its incidence and prevalence is higher in elderly patients [25,26]. The risk of ICH is doubled for each decade after 50 years of age, reaching a maximum at 85 years [27]. On the other hand, hypertension is the most significant modifiable risk factor for acute hemorrhagic cerebrovascular events [21,28], nevertheless other important risk factors are: history of acute myocardial infarction (AMI), antithrombotic therapy, gender, smoking, alcohol consumption, drug abuse, dyslipidemia and diabetes mellitus (DM) [10,29,30].

Hematoma expansion following the event, cerebral edema, seizures, hyperglycemia, pneumonia, fever and sepsis, are the main complications of ICH, and are also considered the main prognostic factors for early mortality in these patients [31]. Despite the seriousness of this condition, therapeutic alternatives for hemorrhagic stroke are few and do not improve the patient´s prognosis. Evidence regarding treatment options for complications is also scarce [32].

Considering the burden acute hemorrhagic cerebrovascular disease has in our region, this study seeks to determine the main clinical and socio-demographic characteristics of patients diagnosed with ICH and treated at the Stroke Unit (SU) in San Juan de Dios Hospital (HSJD), a main adult referral center part of Costa Rica´s National Social Security Health System (CCSS) between the years 2011 and 2015.

Materials and Methods

A retrospective, observational study was performed of medical records in previously diagnosed ICH patients with a documented of well defined, spontaneous and non-traumatic arterial hemorrhage, treated at the SU of the Neurology Department in HSJD (third level referral hospital) of CCSS, from the years 2011 to 2015. Patients with the following characteristics were excluded from analysis in this study: previous modified Rankin Scale Score equal or greater than 3, requirement of mechanical ventilation immediately after the event, indication for surgical treatment, evidence of a subarachnoid hemorrhage and patients under 13 years of age since they are not treated at the SU.

Variables analyzed were classified into 5 groups: socio-demographic aspects, risk factors, management in the prehospital setting, event and in-hospital characteristics. Within the socio-demographic aspects, the following were considered: age, sex, educational level and working condition. The risk factors analyzed were: HT, antithrombotic therapy, smoking, dyslipidemia, DM and history of recent AMI or stroke. Regarding medical management in the prehospital setting, the following were assessed: details regarding the time of the event, emergency telephone 911 intervention and prior management in another healthcare center. The variables studied as part of the event´s characteristics included: causality, hemorrhage location and modified Rankin Scale Score (at 0 and 3 months). In relation to the hospitalization; length of hospital stay (LOS) at the SU, complication rate, in-hospital mortality and post-discharge destination were analyzed.

Absolute and relative frequencies of categorical variables and central tendency measures and dispersion for quantitative variables were determined. Categorical data analysis was done using chi-square test or Fisher's exact test, for quantitative variables differences between means were assessed using Student's t-test or ANOVA test after checking for normality and homoscedasticity. If these assumptions were unmet, non-parametric tests and a *post hoc* analysis were performed. All analyses were determined using SPSS v22.0. (SPSS, Inc., Armonk, NY) and a p-value <0.05 was considered statistically significant. Graphics were prepared using Sigmaplot v11.0 (Systat Software, San Jose, CA). The present protocol was carried out in compliance with all ethical international and national standards and was approved by the Ethics Committee of HSJD, CCSS.

Results and Discussion

Results

The medical records of 74 ICH patients were identified who were treated at the SU, HSJD (CCSS) between 2011 and 2015. This corresponds to 9.4% of all acute cerebrovascular events managed in the Unit during the study period.

The mean age for patients at the time of the event was 64.4 ± 12.6 years, with a range between 40 and 94 years of age. More than 50% (n = 40) of the cases occurred in patients between the ages of 60 and 84 years and in 94.6% (n = 70) of the cases the patients had an age greater than 45 years. The average age of men was lower than the age of women at the time of the event: 62.9 ± 12.4 versus 67.0 ± 11.8 years respectively; however, this difference was not considered significant. Socio-demographically, the population is composed mainly of men in a ratio of 1.75:1 (men:women) (Table 1). However, this ratio varies with age: before 45 years of age the ratio men:women is 4:1, between 46 and 64 years 1.92:1, for ages over 65 and up to 84 years the identified ratio was 1.39: 1 and after 85 years of age it reached a ratio of 1:1.

Sex	Male	47 (63.5%)
	Female	27 (36.5%)
Age (years)	Median ± SD (years) : 64.4 ± 12,6	
	< 45	4 (5.5%)
	45 - 54	13 (17.8%)
	55 - 64	21 (28.8%)
	65 - 74	18 (24.7%)
	75 - 84	12 (16.4%)
	84	5 (6.8%)
Educational Level [a]	Without formal education	4 (7.3%)
	Basic	29 (52.8%)
	Medium	14 (25.4%)
	Higher	8 (14.5%)
Employment Condition	Active	19 (28.8%)
	Home maker	14 (21.2%)
	Retired	22 (33.3%)
	Unemployed	11 (16.7%)

Table 1: Sociodemographic characteristics of patients with an intracerebral hemorrhagic event treated in the Stroke Unit of HSJD, CCSS from the years, 2011 to 2015.
If not stated otherwise, values reflect quantity and percentage
SD: Standard Deviation.
a: In the categories: basic, medium and higher, incomplete education has be included.

At the time of the event, most of the patients showed a basic level of education. Regarding the employment condition, most of the patients were retired, followed by those who had an active working status, those with a homemaker status and finally those who were unemployed. When considering this variable, a significant difference regarding age was observed (p < 0.001), working patients were younger than patients without an active working condition. Male patients predominated among those with an active work condition (Table 1).

All patients (n = 74) showed at least one of the determined risk factors for ICH and in 68.9% (n = 51) of the cases two or more risk factors were identified. The median number of risk factors observed was 2, with an interquartile range (IQR) of 2, a minimum of 1 and a maximum of 6. There was no significant difference between the number of risk factors in relation to sex, age or the educational level of the patients.

Present in 87.8% (n = 65) of the study population, HT was the risk factor with the highest prevalence, followed by a history of smoking in 39.1% (n = 27) of the cases, dyslipidemia 35.4% (n = 22), antithrombotic therapy use 24.3% (n = 18), DM 20.5% (n = 15) and history of a previous AMI or stroke in 15.9% (n = 10). Although hypertension is recorded as a risk factor in such a high percentage, only 13.8% (n = 9) of all hypertensive patients referred an adequate compliance regarding daily usage of antihypertensive treatment at the time of ICH event. 59.1% (n = 13) of the patients with dyslipidemia received treatment at the time of the event, as well as 20.0% (n = 3) of all diabetic patients (Figure 1).
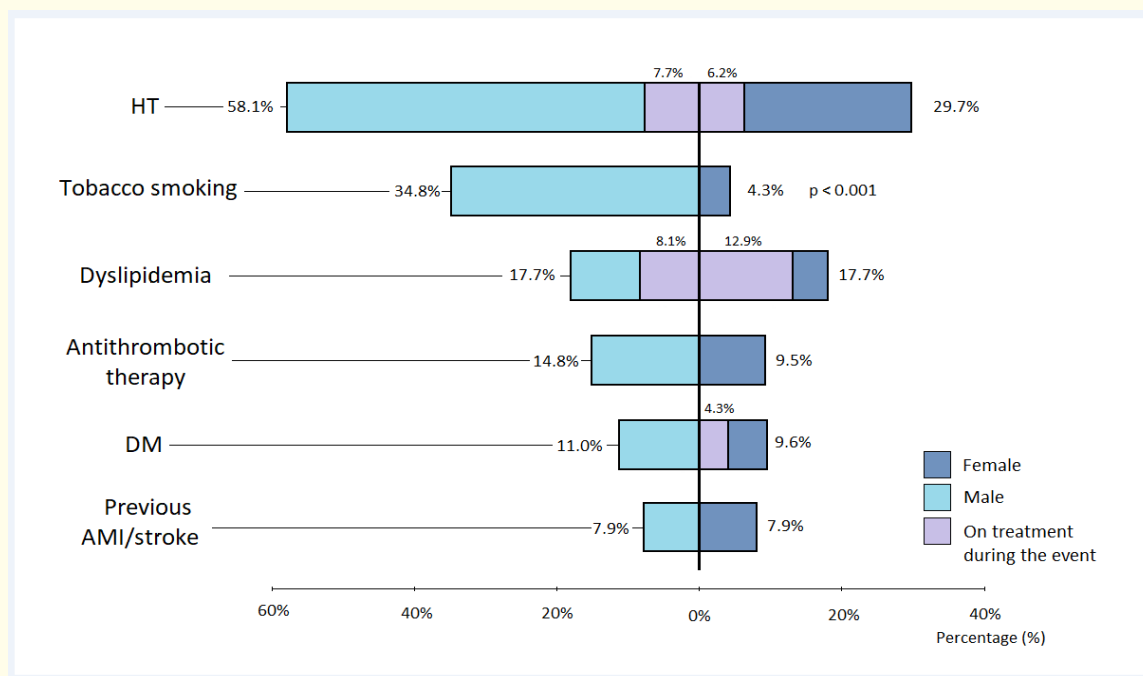

Figure 1: Risk factors according to sex and treatment status of ICH patients.
HT: Hypertension; DM: Diabetes Mellitus; AMI: Acute Myocardial Infarct.

Except for smoking status, in which a direct, proportional, statistically significant moderate to strong (r_{φ} = 0.419) association to the male sex was observed (OR 10.95 95% confidence interval 2.87 - 41.7, p = 0.0005); risk factors such as HT, dyslipidemia, use of antithrombotic treatment, DM and previous AMI or stroke and sex did not show significant associations different from what can be expected due to random occurrence. Nevertheless, HT, antithrombotic use, and DM were more frequently observed in male patients (Figure 1).

In 62.5% (n = 40) of the cases, in which the time of the event was registered, the ICH occurred during the day (mainly during morning hours), 32.8% (n = 21) used the emergency medical service 911 and 46.9% (n= 30) registered a prior admission to a first or second level healthcare center. On the other hand, of the 85% (n = 63) of patients who had a documented cause for their ICH, 90.5% (n = 57) were associated to small vessel disease related to hypertension, followed by those of unknown cause. No difference was observed between the cause of the event and male or female sex (Figure 2). Regarding the events where the localization of the hemorrhage was recorded, 81.0% (n = 47) correspond to deep ICH, including thalamus (31.9%), basal ganglia (27.6%) and internal capsule (19.1%), as the most affected areas (Figure 2). Lobar hemorrhages account for 19.0% (n = 11) of the cases.
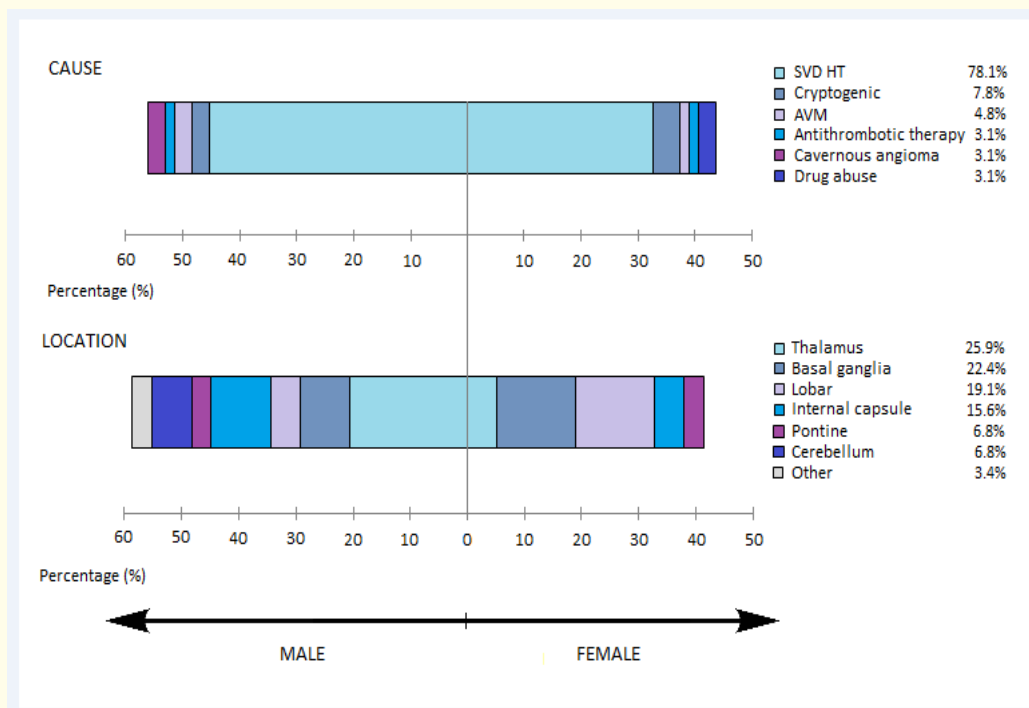

Figure 2: *Cause and location of ICH according to sex.*

ICH: Intracerebral Hemorrhage; SVD: Small Vessel Disease; HT: Hypertension; AVM: Arteriovenous Malformation.

The median regarding the modified Rankin Scale Score (mRS) at the time of the event was 0, both quartiles are equal to 0 and the maximum value is 2, while the median at 3 months was 3, with an IQR of 3. A significant positive and moderate (ρ = 0.633) correlation (p < 0.001) was identified between the patient's age and the mRS score at 3 months (mRS-3M). When dividing the patients according to the mRS-3M (0-1, 2-3, and 4 or more), a statistical difference was observed regarding the patient's age at the time of the event (p = 0.002), the mRS-3M group of 4 or more, evidenced the highest age (72.0 +13.8 years). Only in the first group (0-1) a significant difference in age when compared to sex (p = 0.03) was observed, this being higher in women.

The average LOS in the SU was 7.39 ± 4.72 days, with a median of 6 days and a range between 1 and 26 days. Although the average LOS is almost one day longer in women, 7.88 ± 4.30, compared to men, 7.00 ± 4.94, this difference was not statistically significant.

No significant relationships were identified between LOS and patient's age or the amount of risk factors at the time of the event. Around one fourth of the patients 27.0% (n = 20), continued in hospital care after being discharged from the SU, and the main post-discharge destination for patients was their home 89.3% (n = 50).

Twenty three percent (n = 17) of the patients presented at least one complication during their stay at the SU, 4.0% (n = 3) showed two complications and 1.4% (n = 1) four complications were identified. Even though more complications were observed in male patients (Figure 3), no statistical difference was shown. Also, no correlation was observed between the number of complications and the patient's age or LOS.
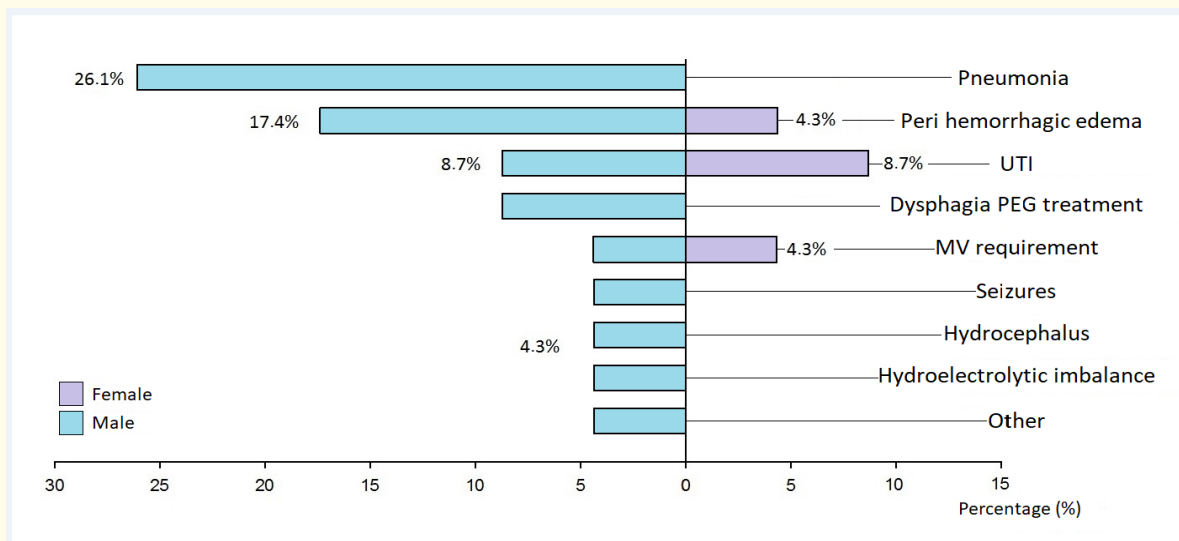

Figure 3: *Complications during SU stay of ICH patients according to sex.*
PEG: Percutaneous Endoscopic Gastrostomy; MV: Mechanical Ventilation; UTI: Urinary Tract Infection.

The main complications reported during the SU hospitalization were: pneumonia, peri-hemorrhagic cerebral edema, urinary tract infections, dysphagia that required a percutaneous endoscopic gastrostomy tube placement and the need for mechanical ventilation. Other complications include: seizures, acute obstructive hydrocephalus and skin pressure ulcers (Figure 3).

Ninety-day mortality was 16.2% (n = 12), 8.1% (n = 6) of patients died during their SU stay, a statistical significant difference was observed between mortality and patient's age (p = 0.006), where patients who died in the hospital setting were on average older. More than 80% of patients (n = 5) who died during the hospitalization had at least one complication, showing a significant association between mortality and the number of complications during hospitalization (p < 0.001).

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Death during the SU hospitalization showed no relationship with the number of risk factors or patient´s sex. However, the difference between LOS in patients who died or not, is greater than what would be expected by chance (p = 0.008), specifically patients who died during the SU stay presented shorter hospital stays.

The majority of deaths in ICH patients were associated with neurological causes, mainly complications due to peri-hematomal edema and consequent increase in intracranial pressure.

Discussion

In this study, similar to what has been identified in other Latin American populations with predominance of European ancestry; it is observed that ICH constitutes around 10% of all acute cerebrovascular events [33]. These figures are very similar to those reported in other countries in the western hemisphere, where spontaneous non-aneurysmal ICH accounts for 10 - 15% of all strokes [21,34].

In broad terms, stroke research shows a statistical significant difference between the age of ICH event and male or female sex, occurring at an earlier age in the male population [35]. In the present investigation, even though there is trend regarding a lower age at the time of the event in the male population, this was not significant. In ICH specially when considering ethnical groups, variations in sex differences have been reported [35-37]. Similar to our case, statistical differences have been not found relating age at the time of the ICH in male or female sex when considering ethnicity [38,39].

The average age of the patients identified in this study when the ICH event occurred, is similar to the age reported in other comparable investigations carried out in nearby latitudes [40-42]. Our study population had a higher ICH incidence in males less than 85 years old, reflecting a greater ICH susceptibility for the male sex. This result is consistent with that reported in studies from other regions of the world, including Europe, Australia and Asia. After 80 years of age, the frequency of ICH in the female population increases and the relation between both sexes reaches a similarity, this behavior between male and female ICH incidence is evident in the present investigation [43-46].

It has been reported that lesser educational level leading to a lower socioeconomic status relates to a higher probability of vascular diseases [47], thus an increase in the educational level associates with lower ICH risk [48,49]. This situation could explain the greater percentage of patients with a basic educational level observed in the present investigation, aspect that could also be influenced by the characteristics of the population assigned to the specific healthcare center. Regarding employment, due to average age in which the ICH occurs, it is expected, as observed in the present study, that most of the patients were retired. In turn, we observe as in other studies, that an active employment condition occurs at younger ages in which the greater proportion of workers belong to the male population [50].

Analogous to the majority of studies, hypertension was identified as the modifiable risk factor for ICH with the highest prevalence [12,21]. It has been reported that hypertension can affect more than 80% of patients with ICH and the majority of patients do not have antihypertensive treatment or lack a hypertension diagnosis at the time of the event [51], aspects clearly confirmed in the present investigation. Other risk factors identified in the present study such as: tobacco smoking, dyslipidemia, antithrombotic therapy use, DM, previous AMI or stroke, are also the major reported conditions that increase the probability of presenting an ICH [28,52,53]. As in other studies, only tobacco smoking as a risk factor in CVD, associates with the sex of the patient [39], this association with the male population has been described elsewhere and occurs independently both in the hemorrhagic or ischemic nature of the stroke [35,54-56]. The higher tobacco consumption observed in males probably reflects both cultural and behavioral differences rather than a specific *per se* risk factor.

Previous studies have published consistent reports on a higher diurnal pattern and a morning peak in ICH events [57,58], this study supports these findings, attributable to the circadian variations in blood pressure [59].

Regardless of the nature of the vascular event, other research suggests that less than half of stroke patients use emergency transportation services and are taken to the hospital by ambulance [50,60,61], an aspect that was observed in the present investigation and one that varies regionally due to a marked educational and cultural influence [62].

Lobar ICH accounts for 14 to 39% of all types of intracerebral hemorrhages [63-66], although in this study the percentage of lobar ICH is within the established data reported worldwide, it is closer to the lower value, this could be explained by the large number of hypertensive patients, and previously identified risk factors for lobar and deep ICH [48,67-69]. In regard with deep ICH as has been described in other studies, our investigation revealed the highest percentage occurring in the thalamus, basal ganglia and internal capsule [36,70,71].

The association found between the patient's age and mRS-3M or mortality has been documented in several published studies [72-77], where findings indicate, as well as in this study, that advanced age and a greater number of complications is associated with a higher early mortality rate. Also, an older age at the time of the event was associated with an unfavorable functional outcome and a decrease in long-term survival, an aspect we could verify by identifying the positive correlation between age and mRS-3M and by comparing the age of patients with mRS-3M scores [78].

The LOS at the SU in patients who suffered from ICH, determined in the present investigation, are similar to what has been reported in other investigations [39, 42, 79-81]. Most published studies conclude that the average hospital stay is related to the severity of the event and the presentation of complications.

The percentage of patients with an ICH event who develop medical complications during hospitalization in the SU is very similar to recently reported data [82], in the same way, the main complications observed compare to what is described in literature in our region [31,42], where infections and cerebral edema are the main medical complications experienced by these patients after CVD. Differences in the rate of complications according to sex and age at the time of the ICH event were not observed in the present investigation, which could be related to ethnic factors as well as to the size of the population analyzed.

The mortality data for patients who suffer an ICH event is quite heterogeneous, figures range from 16.2% to 51.8% [44], in our study, both mortality percentages identified were lower than those reported elsewhere which can be related to: the nature of the population analyzed, which obeys to the medical management given to patients (poor clinical outcome patients at admission are sometimes attended at the neurosurgical intensive care unit) and the size of the population.

For ICH, the data suggesting a difference in the mortality rate by female or male sex is quite contradictory [16,39,43], suggesting a strong interaction from other factors. In the present investigation, the absence of a difference regarding mortality and sex would be in accordance with previous published data. A shorter hospital stay for patients who died, was identified in the present investigation, which can be related to the fact that half of the deaths in an ICH event occur in the first 48 to 72 hours [83].

Conclusion

Despite the differences found attributable mainly to ethnic aspects and the therapeutic approach of stroke patient population attended at this referral medical center; the socio-demographic aspects, risk factors, management in the prehospital setting, event properties and in-hospital characteristics of the studied population resemble what has been described elsewhere.

Current relevance of this research is based on the need to gather information from a specialized reference hospital in Latin America regarding the characteristics of a condition poorly described in the region, also the need to conduct research in this topic has been suggested as a priority in previous published articles [8,35,42,56]. While the main limitations for this study would be its retrospective nature and therefore, the possible inclusion of medical records with heterogeneous data and/or incomplete information. Also, to be considered, the realization in a single, tertiary care center and the nature of the population analyzed could mean that our results cannot be extrapolated to another population.

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