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VARIA

The seasonal incidence of intracranial hemorrhages

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Abstract: *Objective: Cerebrovascular Accidents (CVAs) represent the second most prominent cause of death globally, surpassed only by ischemic heart diseases, thus constituting a significant economic burden for healthcare systems. Despite this, little is known about the correlation between the different times of the year and intracerebral hemorrhages. This review investigates said link, as well as seek to identify whether vascular risk factors (i.e. diabetes and high blood pressure) vary through seasons.*

Method: This paper undertakes the study of 97 patients, all of whom have suffered a hemorrhagic CVA and were hospitalized and treated within the Central Military Emergency University Hospital's Department of Neurology in Bucharest, in the period between 29th of June, 2017 and 29th of July, 2019. The scope of this study is to optimize prophylaxis within the groups most susceptible to the imminent danger of an intracranial hemorrhage during a certain season.

Results: Our study has shown that the season with the highest values of morbidity and mortality is autumn, followed closely by spring.

Conclusion: Given the set of yielded data, which is mirrored in the case of risk factors, we conclude that the results vary slightly from those put forward in the literature. Therefore, whilst hemorrhaging CVAs have a consequential impact upon society, both through the disastrous effects of the incident per se, and its disabling nature in the long-term, a positive percentage of them could be avoided by changing one's behavior during the high-risk periods.

Keywords: *intracranial hemorrhages, subarachnoid hemorrhage, subdural hematoma, hypertension, diabetes mellitus*

INTRODUCTION

Intracranial hemorrhage (ICH) is caused either by tearing apart several small penetrating vessels or as a result of some vascular anomalies. Risk factors such as high blood pressure (HBP) or diabetes mellitus (DM) are frequently associated with ICHs [1, 2]. While in developed countries, the incidence of this pathological condition has reduced due to better control of HBP, in developing countries, it has remained alarmingly constant for the past decades [3].

According to the WHO (World Health Organization), approximately 6 million deaths were attributed globally to ICH in 2016 [4]. In the context of its economic impact, in the US alone, in 2012, the total costs of stroke patients reached USD 71.5 billion, according to the AHA/ASA (American Heart

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Association/American Stroke Association). By 2030, these costs are estimated to reach USD 240 billion [5].

Intracerebral hemorrhages account for approximately 10 to 20% of all strokes [3]. The main cause of developing ICH is the alteration of the structure of the blood vessel caliber as a result of an untreated or inadequately treated chronic high blood pressure (HBP). Other incriminating causes include amyloid angiopathy and vascular malformations. It has been observed that the frequency of ICHs in developing countries is almost double that of developed countries, progressively growing with aging. Ergo, it has been determined that for the 35-54 age group, the incidence is of 6 cases for every 100,000 people, for the 54-74 age group, it increases to 37 for every 100,000 people, and, for the 75-94 age group, it peaks at 176 for every 100,000 people.

For young patients, the main cause of hemorrhages is represented by vascular malformations. In adults, this is represented by chronic HBP, whereas in the elderly, it is amyloid angiopathy. Moreover, it has been shown that, on average, regardless of age, the incidence of ICH is higher in men than in women [6].

Concerning chronic HBP, this leads, eventually, to hypertensive angiopathy which, in turn, causes degenerative modifications within the caliber of the small and medium penetrating vessels, modifications known as lipohyalinosis. Regarding chronic hypertension, it has been ascertained that degeneration takes place at the muscular layer, together with the fibrinoid necrosis of the subendothelial layer, accompanied by micro-aneurysms.

Amyloid angiopathy is characterized by deposits of β-amyloid peptide (βA) in the capillaries, arterioles, and, generally, in all small and medium vessels in the cerebral cortex, leptomeninges, and cerebellum [6]. Secondly, amyloid angiopathy is portrayed through deposits of intravascular βA in the leptomeningeal collaterals and small intracortical vessels. Although the mechanism of depositing and accumulating βA is unknown, its consequence is the degeneration of the blood vessel caliber through, more specifically, losing smooth muscle fibers, thinning the caliber, narrowing the lumen, and leading to aneurisms, the latter further giving birth to diffuse micro-hemorrhages [7].

Furthermore, apart from HBP, other causes include the dysfunction of self-regulating with excessive cerebral blood flow, arteriovenous malformations, ruptured aneurysms, cerebral angiopathy, hemorrhagic necrosis, cerebral venous thrombosis, and modified hemostasis.

The overflow of the resulting blood from the bursting of the caliber leads to a sudden increase of intracranial pressure, which brings about diffuse vasospasm, followed by the acute ischemia of the parenchyma – a mechanism which is frequently present in the potential vasospasm after subarachnoid hemorrhage [8, 9]. The BBB permeability heightens, thus aggravating the metabolic disorders of the brain, giving birth to the cerebral edema [10]. Despite the advancements in medicine, cerebral bleedings have retained a status of high morbidity and incremental mortality, unaddressed properly by the modern therapeutic methods developed hitherto. This is partly due to the complex, irreversible pathophysiology processes which occur the moment blood makes contact with the cerebral parenchyma. Understanding this phenomenon and ICH's evolution would allow identification of the potential therapeutic targets.

METHODS

A retrospective study has been conducted which includes patients who have had non-traumatic hemorrhaging vascular accidents, hospitalized and treated in the period between June 2017 and July 2019 within the "Carol Davila" Central Military Emergency University Hospital's Department of Neurology.

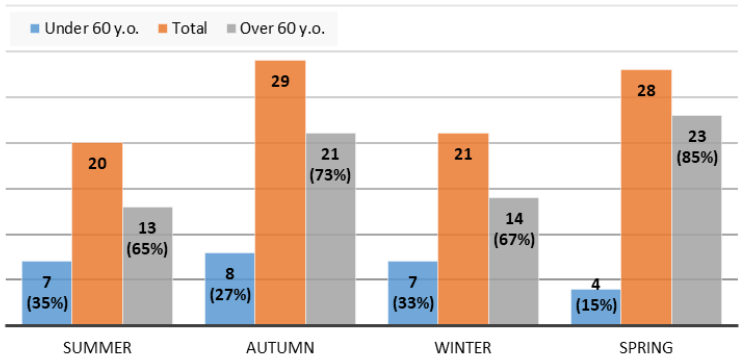
The selected patients have been diagnosed with non-traumatic intracerebral hemorrhage by a neurologist, subsequently confirmed through a CT scan. The patients' age varied between 23 and 97 years, with provenance from both countryside and urban environment, with diverse professional occupations. We have investigated the three main types of non-traumatic bleedings, namely, intraparenchymal hemorrhage (IPH), subarachnoid hemorrhage (SAH), and subdural hematoma (SDH).

RESULTS

Out of the 97 patients, 67% were male and 33% female. Out of these, as many as 77% have presented non-traumatic IPH, 13% SAH, and 10% SDH. 17% of the patients have deceased during hospitalization. The average age was 67 years old, 72% of those placed in medical care being older than 60 years old (Figure 1). The average period of hospitalization was 21 days, with a minimum of 2 days and a maximum of 587.

Seasons were defined in the same way as in the rest of the studies, to have a consistency between these, for the sake of comparing them and display our research as suitable, i.e. summer: 1st of June – 31st of August, autumn: 1st of September – 30th of November, winter: 1st of December – 28/29th of February, spring: 1st of March – 31st of May.

We have identified an incremental occurrence of the cases of cerebral hemorrhages in transitional seasons, namely, autumn and spring. Similar results have been produced in most of the past studies, regardless of whether, in some situations, these have shown a larger incidence in winter (based on the geographical areas where these have been carried out) due to the physiological differences of organisms at low temperatures [11, 12, 13].

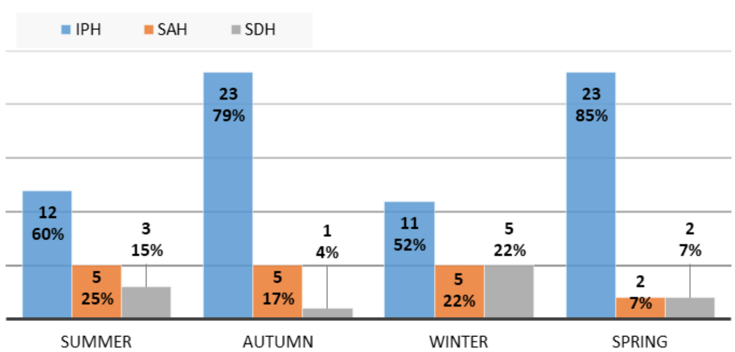


Legend: blue – the incidence of intracerebral hemorrhage (ICH) in the under 60 age group; orange – total incidence of both age groups; grey – the incidence of ICH in the over 60 age group

Figure 1: Number of cases (percentage) of ICH's seasonal incidence

Concerning the seasonal incidence of each type of hemorrhage (Figure 2), we observe an increase in IPH in autumn and spring, a constant incidence in SAH in summer, autumn, and winter, with a lower number of cases in spring, and a relatively constant number for SDH, with a maximum and a minimum number of cases in winter and autumn, respectively.

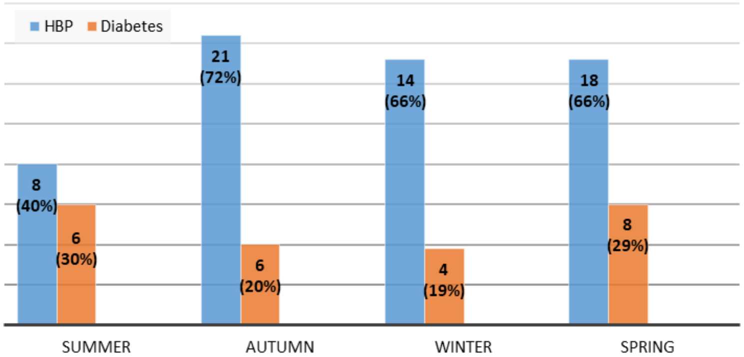
It is widely accepted that the main risk factor of ICH is represented by chronic HBP, corroborated with a hypertensive leap exceeding the limit of cerebral vascular resistance. The risk of hemorrhage in hypertensive patients is 1.5 times for BP ~ 140 mmHG and three times for BP > 180 mmHg than it is for normotensive patients [14].



Legend: blue – frequency of intraparenchymal hemorrhage (IPH), orange – the incidence of non-traumatic subarachnoid hemorrhage (SAH); grey – the incidence of subdural hematoma (SDH)

Figure 2: Seasonal incidence of hemorrhages

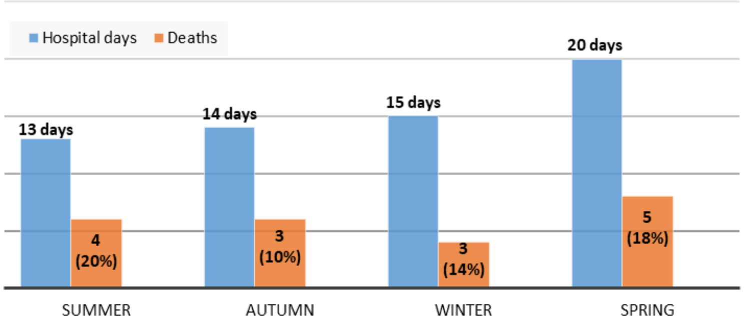
Out of all diagnosed with IPH, 27% out of the 73 patients have had no associated diabetes mellitus (DM) or chronic HBP, 70% suffered from chronic HBP, 20% from diabetes, and 18% from both. In the context of SAH, 61% had no associated comorbidities, 31% had chronic HBP, 15% DM, and 7% both chronic HBP and DM. Out of those who have been hospitalized from non-traumatic SDH, 36% have not shown any of the abovementioned risk factors, 54% have shown HBP, 27% DM and 18% have shown both. In the analyzed lot, 61 patients suffered from HBP in different degrees, this number representing 62% of the hospitalized patients. The highest rate of cerebral bleedings associated with chronic HBP was registered in autumn, followed by spring (Figure 3). Besides this, we have also evaluated the association between DM and cerebral hemorrhage, as DM may determine an unpropitious prognostic in the case of ICH. Persons with diabetes have a 20% increased risk of suffering from cerebral bleeding, as opposed to a person not afflicted, as well as over a 50% chance of dying within 30 days after the hemorrhage [15]. In our study, we have identified a prevalence of diabetes of 29% among hospitalized patients.



Legend: blue – the prevalence of high blood pressure (HBP) at ICH patients; orange – the prevalence of diabetes mellitus (DM) at ICH patients.

Figure 3: HBP and DM

According to this data, we observe that, indeed, diabetes does not seem to play an important role in contributing to ICH, yet there is high morbidity during summer and winter, seasons with extreme temperatures, and low morbidity during the transitional seasons, spring and autumn. Moreover, there is a higher risk of cerebral hemorrhaging during winter and summer, for those who have diabetes as an associated pathological condition. Apart from a heightened incidence of ICH in spring, we emphasize the more severe nature of these through lengthy hospitalizations periods, hence the increased economic burden on healthcare systems (Figure 4). Considering the number of days of hospitalization as an indicator of the gravity of the hemorrhage, as well as its occurrence in critical areas or through associated complications, we must submit a longer period of recovery for these patients and a lower degree of autonomy and social reintegration. Concerning deaths, we observe a relatively constant rate throughout the entire year, thus barring us from claiming any one risk factor in particular increases ICH's mortality. Apart from the increased morbidity, spring also registers the highest rates of mortality.



Legend: blue – the average number of hospital days; orange – number of deaths

Figure 4: Hospitalization and deaths

DISCUSSIONS

The results of this study show a variety of the incidence of hospitalization, in-hospital mortality, duration of hospitalization, and patients' prognostic throughout the year, in Bucharest, a region with a temperate continental climate. The data is new for this geographic zone, as, hitherto, there have been no recorded statistical studies (at least recent) to quantify the seasonal incidence of ICH in this area. Consequently, this research tackles on a novel theme, representing a pilot study. For the patients included in this study, the highest incidence was observed during the transitional seasons, especially during autumn, whereas the lowest was during summer. The yielded results contradict the larger part of studies available in the specialized literature, which have either failed to find a variety of incidence or claimed a heightened incidence in other seasons, particularly in winter and spring [12, 13, 16, 17]. Nonetheless, there are also similar results [11].

Regarding the seasonal distribution on age groups, the current study has registered a constant tendency of ICH debuting at patients under 60 throughout the year, apart from spring, when it has decreased, contrary to the constant incidence in the year evaluated by other studies [11, 12]. Conversely, regarding patients over 60, the seasons corresponding to high risk are spring and autumn, with two minimums registered during winter and summer, data which is in line with the results of other comparative studies [11, 12].

When the assessment also includes comorbidities, data is similar to that obtained in other research papers. Diabetes does not seem to play a decisive role in how a hemorrhage comes to be, but it may exacerbate the prognostic [15]. On the other hand, concerning HBP, this is seen as being the most important risk factor for hemorrhage and it has implications both for the prognostic and survival [18]. The mechanisms underlying these seasonal varying conditions are not clear, but it is probable for the latter to be associated with seasonal variations in biological factors, such as the level of serum lipids, some components of the blood, and a hypercoagulable state [19]. Concerning the number of deaths, we have not observed a significant variation in the year, thus being relatively constant, similar data having been obtained by other authors as well [12, 13].

The reason why the risk of ICH is modified throughout the year is not entirely known. The dysfunction of the environmentally adaptive physiological processes may be the underlying cause of hemorrhages. Variations in temperature and atmospheric humidity are considered the main catalyst for hemorrhaging events [20]. Low temperatures and low atmospheric humidity can increase evaporation, leading to an increased demand for salt, thus constituting HBP [20].

CONCLUSIONS

ICH is one of the most important neurological pathological conditions. Even though incidence is lower than it is in the case of ischemic strokes, morbidity and mortality are higher. There is still an ongoing need for thorough studies regarding the seasonal incidence of cerebral hemorrhages, as there is a subset of modifiable factors related to behavior and lifestyle which can potentially contribute to avoiding a hemorrhagic episode in either one of the seasons.

In this study, we have noticed a heightened tendency to cerebral bleeding during autumn and spring, as compared to other geographic zones or climates. Moreover, we have seasonally classified the type of ICH patients in this study were subject to, observing the predominant IPH throughout the entire year. We have also determined the average number of necessary hospital days for each season, emphasizing that spring is associated with the highest morbidity. Furthermore, in the context of this study, we have also found a significant correlation between chronic HBP and the incidence of cerebral hemorrhages, confirmed prior data that DM is a risk factor for triggering a hemorrhagic stroke, but with no real influence on mortality, as well as defined seasonal risk of ICH groups based on age and comorbidities.

In the future, it is paramount that we understand better the physiopathological process underlying cerebral hemorrhages to develop efficient methods with therapeutic potential. Although this may seem ideal, reducing seasonal incidence in risk groups through educating patients is particularly difficult to achieve. Until then, developing methods of treatment that focus on slowing down or completely barring the inflammation's progress and, implicitly, that of neurological deficits, is a short-term objective.

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