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Original Scientific Paper

METEOROLOGICAL VARIABLES ASSOCIATED WITH SUBARACHNOID HEMORRHAGE: A SINGLE CENTER STUDY

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SUMMARY – Spontaneous subarachnoid hemorrhage (SAH) can occur unexpectedly and independently of the classic risk factors. Several different factors could affect intracranial aneurysm (IA) rupture, such as morphological and hemodynamic factors. The aim of this study was to establish the potential association of meteorological data such as temperature, atmospheric pressure, and humidity, and the onset of clinical symptoms preceding hospital admission of patients with acute SAH due to IA rupture. This retrospective study included 130 consecutive patients admitted for non-traumatic SAH with a determinable onset of SAH symptoms. The effects of meteorological parameters of atmospheric pressure, ambient temperature, and relative air humidity on the day of acute SAH onset and 24 hours prior to the onset of symptoms were recorded and analyzed in each patient. Spearman rank correlation analysis was used to assess the risks of incident SAH on the basis of daily meteorological data. Seasonal incidence of acute SAH showed the peak incidence in winter and a trough in summer, with monthly incidence peak in January and December. The circadian rhythm analysis showed the peak incidence of SAH in the forenoon, followed by the evening. Acute SAH incidence showed moderate positive association with daily atmospheric pressure ($p<0.05$), while no association was found with ambient temperature and relative air humidity. Our results suggested no significant association of changes in ambient temperature and relative humidity with the risk of SAH. Increases in atmospheric pressure were weakly associated with a higher SAH risk. Additional studies are needed to establish in detail both meteorological and morphological factors important to predict IA rupture and SAH.

Key words: *Meteorological variables; Subarachnoid hemorrhages; Intracranial aneurysms*

Introduction

Spontaneous subarachnoid hemorrhage (SAH) is a major condition with the annual incidence of approximately 91 *per* 100 000. The vast majority of SAH cases, around 85%, are caused by intracranial aneurysm (IA) rupture, which is one of the most serious complications associated with aneurysms. Morbidity and mortality of aneurysmal SAH remain high[1,2]. Approximately one-third of all patients suffering from SAH do not survive the first month after initial incident, while half of the survivors remain disabled[1,3]. Although case fatality of SAH from a ruptured IA has decreased over the last

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decades, further decrease will not be easy to achieve because of the considerable proportion of patients who die before reaching the hospital. In order to create strategies to prevent SAH, detailed insight in the risk factors analysis and the pathophysiology of IA rupture is necessary[4,5].

Therefore, it is critical to understand the risk factors associated with this disease. The mechanisms underlying IA development and the factors associated with IA rupture are not yet fully understood. Several environmental risk factors for IA rupture resulting in SAH are gender, age, region, high blood pressure, smoking, high alcohol intake, female sex, and a family history of IA[5-12]. The mentioned factors discriminate poorly between high and low risk aneurysms, and most SAH occur unexpectedly and independently of these risk factors. In addition, other, extensive studies analyzed morphological factors and differences between ruptured and unruptured IA, such as the size, shape, the neck, etc., as well as hemodynamic factors[13-17].

Furthermore, it was previously suggested and discussed that an additional possible risk factor of IA rupture and SAH could be seasonal or meteorological factors; some studies found that meteorological changes were associated with an increased incidence of SAH[18-26], whereas others report absence of such association[27-31]. When observing and analyzing the data presented, the associations that have been observed appear to be conflicting. Even a recent meta-analysis was not able to determine the association between meteorological factors and SAH due to heterogeneity of data from previously published studies[5]. One of the main uncertainties was whether the relations observed between meteorological factors and SAH incidence were chance findings, or the lack of association in negative studies was caused by too small numbers of included patients to detect the association. Furthermore, published results vary greatly depending on geography, climate, and study design. Therefore, evidence regarding the impact of meteorological factors on the SAH incidence remains a matter of debate.

The aim of this study was to establish the potential association of meteorological data such as temperature, atmospheric pressure, and humidity, and the onset of clinical symptoms preceding hospital admission of patients with acute SAH due to IA rupture. Determining the weather-related risk of SAH can help in IA rupture prediction and improve population health.

Patients and Methods

This retrospective study was conducted at the Department of Neurosurgery and Department of Neurointerventional Radiology, Sestre milosrdnice University Hospital Center, Zagreb, Croatia, from January 1, 2016 till June 1, 2021, with an area coverage of around 200 km. The study included 130 consecutive patients, 87 female and 43 male. Patient data were collected and analyzed from hospital electronic medical records including the patients discharged from the hospital with a diagnosis of SAH (I60.x, International Classification of Diseases, 10th Revision).

Available patient-related medical data including clinical, laboratory and neuroradiological reports were individually analyzed to identify patients diagnosed and treated due to acute SAH. Diagnosis of SAH was confirmed in all included patients using computerized tomography angiography. Additional data obtained from patient files included age, sex, date of onset of symptoms and date of aneurysm rupture and hospital admission, aneurysmal size, the World Federation of Neurological Surgeons grading score for subarachnoid hemorrhage (WFNS) and Fisher grading. Exclusion criteria were as follows: incomplete or inaccessible patient data, history of head trauma of at least 48 hours prior to the onset of clinical symptoms, indeterminable time of clinical symptom onset, and admission due to the reason other than acute SAH.

In addition, geographical location, above sea level and time of symptom onset were recorded for each individual patient. Data on weather conditions and indicators were obtained from the Croatian Meteorological and Hydrological Service (https://meteo.hr/). The following meteorological parameters on the day of acute SAH onset and 24 hours prior to the onset of symptoms in each patient were recorded: daily maximum, minimum and mean ambient temperatures (°C), daily mean relative humidity (%), and daily mean atmospheric pressure (hPa). Changes in these meteorological parameters were calculated as differences between the day of and day before the onset of acute SAH. All data were checked for accuracy by two independent researchers.

Statistical data analysis was performed using MedCalc Statistical Software version 12.5.0 (MedCalc Software, Ostend, Belgium; https://www.medcalc.org). Distribution was assessed by the Kolmogorov-Smirnov test, while χ^2-test was used for qualitative variables. The associations between meteorological parameters and various patient data were assessed by Pearson correlation coefficient or Spearman's rank correlation. The level of statistical significance was set at p<0.05.

Results

Between January 1, 2016 and January 1, 2021, a total of 130 consecutive patients (87 female and 43 male) were included in the study. Patient characteristics are shown in Table 1. The mean age of all patients was 51.51±12.97 years, with 57.91±14.05 in female and 52.01±13.17 in male patients. The highest incidence of aneurysms was recorded in the middle cerebral artery (34/130, 26.15%), followed by the anterior communicating artery (26/130, 20.00%) (Table 1). The rupture rates for aneurysm sizes <7 mm were 68/130 (52.31%), >7 mm 45/130 (34.61%) and undetermined 17/130 (13.07%) (Table 1). The WFNS SAH and Fisher grading were determined in all included patients (Table 1).

We presented data according to months and seasons (winter, spring, summer and fall); additionally, circadian rhythm was analyzed according to the time of acute SAH onset on the basis of the following six 4-hour periods: morning (04:00-07:59), forenoon (08:00-11:59), midday (12:00-15:59), afternoon (16:00-19:59), evening (20:00-23:59), and night (00:00-03:59). Total acute SAH incidence according to seasons, months and time at onset is shown in Table 2.

The peak monthly incidence was in December (18/130) and January (21/130), and the trough monthly incidence was in April, June and August (6/130). The seasonal incidence peaked in winter (December to February, 50/130) and exhibited a trough in summer (June to August, 21/130; p<0.05). The peak incidence of SAH was recorded in the forenoon (08:00-

Table 1. Patient characteristics

Summary statistics	n	%
Total patients	130	100
Sex		
Female	87	67
Male	43	33
Age, years (mean ± SD)	51.51±12.97	
Female	57.91±14.05	
Male	52.01±13.17	
Location of ruptured IA		
ICA	15	11.53
MCA	34	26.15
ACA	16	12.30
PCA	3	2.30
ACoA	26	20.00
PCoA	11	8.46
VBA	3	2.30
Other	22	16.92
Size of ruptured IA		
≤7mm	68	52.31
≥7mm	45	34.61
Undetermined	17	13.07
WFNS		
1-2	84	64.62
3-5	46	35.38
Fisher grading		
1-3 (no intracerebral or intraventricular clots)	48	36.92
4 (intracerebral or intraventricular clots)	82	63.08

IA = intracranial aneurysm; ACA = anterior cerebral artery; AcoA = anterior communicating artery; ICA = internal carotid artery; MCA = middle cerebral artery; PCA = posterior cerebral artery; PCoA = posterior communicating artery; VBA = vertebrobasilar artery; WFNS = World Federation of Neurological Surgeons subarachnoid hemorrhage grading.

Table 2. Month, season and circadian rhythm analysis

Month analysis, n		Season analysis, n		Circadian rhythm analysis, n	
January	21	Winter	50	Morning (04:00-07:59)	9
February	11				
March	10	Spring	24	Forenoon (08:00-11:59)	49
April	6				
May	8			Midday (12:00-15:59)	12
June	6	Summer	21		
July	9			Afternoon (16:00-19:59)	17
August	6				
September	15	Fall	35	Evening (20:00-23:59)	37
October	7				
November	13			Night (00:00-03:59)	6
December	18	Winter	50		

11:59; 49/130), followed by the evening (20:00-23:59; 37/130), whereas the trough was at night (00:00-03:59; 6/130; $p<0.05$).

Daily mean temperature ($r=0.026$, $p<0.58$), daily maximum temperature ($r=0.18$, $p<0.98$), and daily minimum temperature ($r=0.21$, $p<0.12$) showed no association with daily SAH incidence, and so did not daily mean relative humidity either ($r=0.18$, $p=0.21$). Meanwhile, daily mean atmospheric pressure yielded a moderate positive association with acute SAH incidence ($r=0.048$, $p<0.05$).

Next, daily fluctuations in temperature and fluctuations on the day of acute SAH onset and 24 hours prior to the onset of symptoms in each patient showed no association between the incidence of SAH and fluctuations in the factors analyzed.

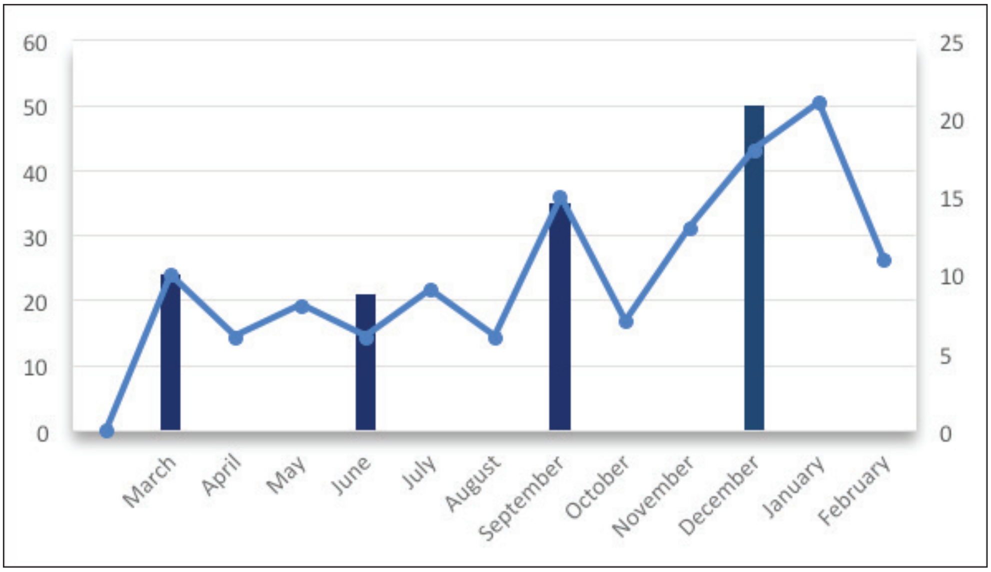

Fig. 1. Seasonal incidence of acute subarachnoid hemorrhage showing the peak incidence in winter (December to February) and a trough in summer (June to August). Monthly incidence peaked in January and December, and the trough monthly incidence was in April, June and August.

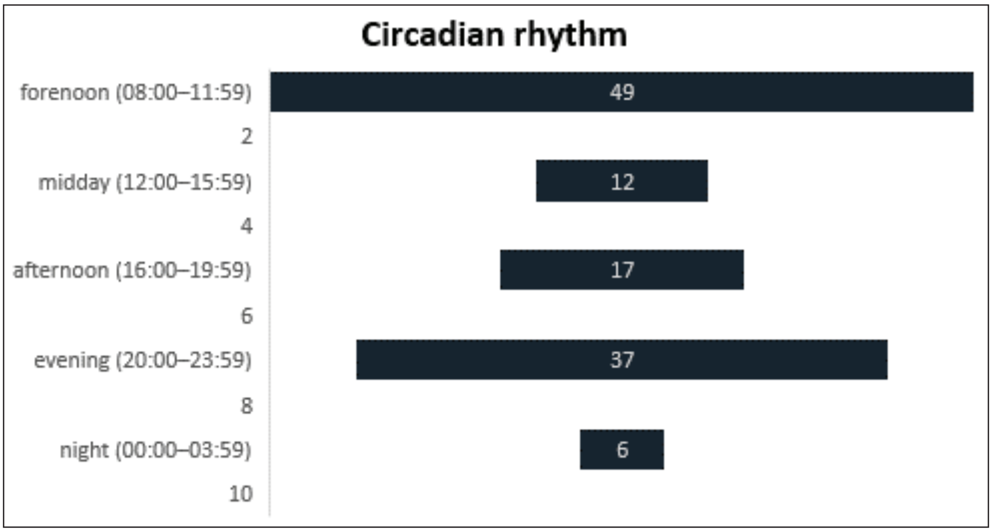

Fig. 2. Circadian rhythm analysis showed the peak incidence of subarachnoid hemorrhage in the forenoon (08:00-11:59; 49/130), followed by the evening (20:00-23:59; 37/130), whereas the trough was at night (00:00-03:59; 6/130; p<0.05).

Discussion

In our study, we aimed to establish the potential association of meteorological data such as temperature, atmospheric pressure and humidity, and the onset of clinical symptoms preceding hospital admission of patients with acute SAH due to IA rupture. The effects of meteorological changes on IA rupture and consequential SAH remain a matter of debate because of the inconsistent findings of studies evaluating the relationship between different weather conditions and SAH incidence.

The peak seasonal and monthly incidence of SAH was highest in winter (January and February), and lowest in spring (April) and summer (June and August) (Fig. 1). Furthermore, circadian rhythm analysis showed the peak incidence of SAH to be significantly higher in the forenoon (37.69%), followed by the evening (28.46%), whereas the trough was at night (4.61%) (Fig. 2).

Additionally, daily mean temperature, daily maximum temperature and daily minimum temperature showed no association with daily SAH incidence, and so did not the mean relative humidity either, while daily mean atmospheric pressure yielded a moderate positive association with acute SAH incidence and hospital admission for ruptured IAs. Meanwhile, daily fluctuations in temperature and relative humidity, as well as fluctuations on the day of acute SAH onset and 24 hours prior to the onset of symptoms showed no association between the incidence of SAH and fluctuations in the factors analyzed.

Low SAH incidence in summer, as observed in our study, has also been reported elsewhere[5,32]. The phenomenon was previously explained by meteorological determinants and the physiological processes they influence. On the contrary, the higher SAH incidence during winter could be explained by various factors. Lower temperatures during winter induce peripheral vasoconstriction leading to increased blood and pulse pressure. High blood pressure is an established risk factor for SAH[32]. The mentioned cascade, especially under abrupt temperature changes, may produce wall deformity and increase friction and shear stress on the IA[5,19,26,33]. In addition, physiological responses to cold during winter, such as increases in platelet and red cell counts, increased sympathetic nerve activity, decreased factor VIII, antithrombin III and platelet aggregation, increased fibrinolytic activity, etc., should be taken into account[5,33]. Furthermore, cold weather leads to altered human behavioral response such as smoking indoors, increased alcohol intake, decreased physical exercise, etc.[5,26].

Although previous studies have reported that temperature changes may increase the SAH incidence[19,21,22,24-26], our results showed no association between temperature changes and SAH incidence. Regarding association between atmospheric change in pressure, these data are inconclusive and controversial. Increased SAH risk has been reported in correlation with increasing atmospheric pressure in different geographical regions[34-40], while other studies report on an increased SAH risk associated with decreased atmospheric pressure[41] or even absence of association[25,27]. There is a significant number of published papers showing some kind of association between atmospheric pressure change and SAH incidence, probably because papers with negative results are rarely published, as pointed previously[31]. Furthermore, several authors speculate that atmospheric pressure may affect blood or intracranial pressure, leading to possible IA rupture[40,42]. Still, at this time, there is no satisfactory explanation for the association between atmospheric pressure changes and SAH.

In only a few studies did humidity correlate with SAH incidence[23,27]. There are no studies that confirm correlation of precipitation and IA rupture. In this study, we did not take into account sunlight exposure. Currently, there are several papers regarding this parameter that show clinical meaningfulness, albeit contradictory[23,43].

Since more factors influence SAH incidence and IA rupture, we have to mention hemodynamic changes that may cause morphological changes and thus play an important role in the occurrence, development and rupture of IA[44,45]. Furthermore, the effect of the combination of meteorological factors, hemodynamic changes and aneurysm morphology on the prediction of IA rupture has not been in depth investigated. Very few studies combined morphological parameters of IA and meteorological variables, indicating that some IA that were not considered likely to rupture may rupture easily in high-risk meteorological conditions[26].

This study had several limitations that should be considered. First, this was a retrospective study. Second, the meteorological data assessed in this study were limited. For the meteorological factors included (temperature, atmospheric pressure, and humidity), values were measured three times a day, i.e., at 7 a.m. and 2 and 9 p.m.; daily mean values were also included in the analysis. This may have weakened assessments of the complexity of meteorological changes. Future studies with large samples and abundant meteorological data will be necessary to overcome these limitations. Finally, our study did not include 6%-14% of patients who died of SAH before reaching the hospital, which could have resulted in underrepresentation of patients with the most severe bleedings[46]. Additionally, we acknowledge the possibility that patients with less severe bleedings were also underrepresented as these patients often present with minor symptoms and are misdiagnosed in approximately 10% of cases[47].

Conclusion

The results presented in this study suggest no significant association between changes of ambient temperature and relative humidity and SAH incidence. In addition, increases in atmospheric pressure were weakly associated with a higher SAH incidence, but the significance of this result remains unclear. Further studies are needed to establish in detail the possible association between meteorological factors in combination with other previously described risk factors, as well as morphological and hemodynamic factors important to predict IA rupture and SAH.

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Sažetak

POVEZANOST METEOROLOŠKIH VARIJABLA SA SUBARAHNOIDNIM KRVARENJEM: ISKUSTVO JEDNOG CENTRA

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Spontano subarahnoidno krvarenje (SAH) može nastati neočekivano i neovisno o klasičnim čimbenicima rizika. Nekoliko različitih čimbenika može utjecati na rupturu intrakranijske aneurizme (IA), poput morfoloških i hemodinamskih čimbenika. Cilj ovoga istraživanja bio je utvrditi potencijalnu povezanost meteoroloških podataka kao što su temperatura, atmosferski tlak i vlažnost te pojave kliničkih simptoma prije prijma u bolnicu bolesnika s akutnim SAH-om zbog rupture IA. Ova retrospektivna studija uključila je 130 uzastopnih bolesnika primljenih zbog netraumatskog SAH-a s vidljivim početkom simptoma SAH-a. Za svakog bolesnika zabilježeni su i analizirani učinci meteoroloških parametara atmosferskog tlaka, temperature okoline i relativne vlažnosti zraka na dan nastanka akutnog SAH-a i 24 sata prije pojave simptoma. Korelacijska Spearmanova analiza primijenjena je za procjenu rizika od incidentnog SAH-a na temelju dnevnih meteoroloških podataka. Sezonska incidencija akutnog SAH-a pokazala je vrhunac incidencije zimi i pad ljeti, s mjesečnim vrhom incidencije u siječnju i prosincu. Analiza cirkadijanog ritma pokazala je vrhunac incidencije SAH-a u prijepodnevnim satima, a zatim navečer. Učestalost akutnog SAH-a pokazala je umjereno pozitivnu povezanost s dnevnim atmosferskim tlakom ($p<0,05$), dok nije nađena povezanost s temperaturom okoline i relativnom vlagom zraka. Naši rezultati ukazuju na to da nema značajne povezanosti promjena u temperaturi okoline i relativnoj vlažnosti s rizikom od SAH-a. Povećanje atmosferskog tlaka slabo je povezano s većim rizikom od SAH-a. Potrebne su dodatne studije kako bi se detaljno utvrdili meteorološki i morfološki čimbenici važni za predviđanje rupture IA i SAH-a.

Ključne riječi: *Meteorološke varijable; Subarahnoidno krvarenje; Intrakranijske aneurizme*