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An Epidemiological Investigation on Patients with Non-traumatic Subarachnoid Hemorrhage from 2010 to 2020

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ABSTRACT

Objective: Subarachnoid hemorrhage (SAH) is still considered a life-threatening medical condition with a high mortality rate, particularly in developing countries. Thus, the present study aimed to investigate the angiographic findings of non-traumatic or spontaneous SAH.
Methods: This retrospective cohort study included 642 health records of patients with non-traumatic SAH over a 10-year period, from 2010 to 2020. The required data, including demographic information, aneurysm type, size, location, disease severity classification, and secondary complications, were extracted.
Results: The study included 642 patients, with 262 (40.8%) being male. The mean age of the participants was 54.72±13.51 years. The most prevalent type of aneurysm was saccular (89.1%), while serpentine (0.2%) and dissecting saccular (0.2%) aneurysms had the least prevalence. The most frequently involved arteries were the anterior communicating artery (ACoA; 38%), internal carotid artery (ICA; 27.6%), and middle cerebral artery (MCA; 13.4%). There was a significant correlation between sex and aneurysms occurring at ACoA and ICA ($p< 0.0001$), and ACoA – A1 ($p=0.02$). Patient age and sex were also significantly correlated with one another ($p<0.0001$). There was no statistically significant correlation between sex, aneurysm size, Glasgow coma scale (GCS), and modified Rankin scale (MRS).
Conclusion: Based on our findings, the presence of aneurysms at ACoA, ACoA – A1, and ICA should be thoroughly ruled out in patients with severe headaches of sudden onset, particularly male patients of younger ages.

Keywords: Subarachnoid hemorrhage; Aneurysm; Complication.

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Introduction

Subarachnoid hemorrhage (SAH) is a medical condition characterized by bleeding in the space between the brain and the dura matter [1]. This condition is classified as a medical emergency due to its potentially life-threatening consequences [2]. It can cause severe neurological damage or even death if not promptly diagnosed and treated [3]. The bleeding in the subarachnoid space can cause an increase in intracranial pressure, which can compress vital structures within the brain, and cause brain injury [4]. Additionally, blood clots may form and obstruct normal blood flow, depriving brain tissue of oxygen and nutrients [5].

Common symptoms of subarachnoid hemorrhage include a sudden severe headache (often described as “the worst headache of my life”), nausea, vomiting, neck stiffness, sensitivity to light (photophobia), seizures, loss of consciousness, or focal neurological deficits such as weakness or numbness in specific body parts [6]. Recognizing these symptoms promptly can help individuals seek immediate medical attention and receive appropriate treatment.

Early diagnosis and treatment are essential for improving outcomes in patients with subarachnoid hemorrhage [7].

Imaging plays a crucial role in the diagnosis of SAH, and useful imaging techniques include computed tomography scans (CTs), CT angiography, magnetic resonance imaging (MRI), and digital subtraction angiography (DSA) [8-10]. Angiography findings in subarachnoid hemorrhage play a crucial role in the diagnosis, management, and prognosis of this potentially life-threatening disease [11].

The size, location, and morphology of aneurysms identified through angiography are essential factors in determining appropriate treatment options [12]. Endovascular techniques, such as coiling or stent-assisted coiling, can be employed during angiography to treat certain aneurysms non-surgically. Furthermore, angiography findings can help in determining the overall prognosis for patients with SAH [13]. The presence of multiple aneurysms or certain characteristics of the aneurysm, such as size, shape, and location, can influence the risk of re-bleeding and subsequent complications. This information is critical for making long-term management decisions and providing appropriate counseling to patients and their families [14].

The present study evaluated the DSA findings of non-traumatic or spontaneous SAH by following patients admitted to a referral hospital from 2010 to 2020.

Material and Methods

From 2010 to 2020, this retrospective cohort research was conducted on the health records of patients admitted to an institutional referral hospital in eastern Mashhad with an initial diagnosis of non-traumatic or spontaneous SAH. This study included all patients suspected of SAH, as well as individuals with a confirmed diagnosis based on the findings of brain CT, LP, or validated by a fellow neurosurgeon.

As this was a retrospective study on patient health records, neither an informed consent was required, nor did we intervene in the treatment of patients.

To evaluate the clinical condition of patients upon admission, they were categorized into several classes using four major classification systems: Fisher, modified Fisher (M Fisher), World Federation of Neurological Surgeons (WFNS) scale, and Modified Rankin Scale (MRS), as shown in Table 1. While the (M) Fisher scales are based on the hemorrhage features, the WFNS system is based on the Glasgow Coma Scale (GCS), and MRS takes into account the patients’ physical competency (Table 1).

The data was analyzed using the SPSS software version 22 (SPSS Inc., Chicago, Illinois, USA). The continuous variables were presented as mean±SD. The Chi-square test was used for the association of sex and location of the aneurysm. The associations among age, aneurysm size, and aneurysm neck size, GCS, and MRS were evaluated using the independent T-test.

Table 1. MRS and WFNS classification systems, are used for categorizing the patients, based on the severity of their condition

Class	Fisher	M Fisher	MRS	WFNS
0			No symptoms	
1	No blood was detected.	Focal or diffuse thin SAH, no IVH [a]	No significant disability, despite some symptoms.	GCS: 15 without neurological deficit
2	Diffuse deposition or thin layer with all vertical layers of blood <1 mm thick	Focal or diffuse thin SAH, with IVH	Slight disability. Able to look out after own affairs without assistance.	GCS: 13–14 without neurological deficit
3	Localized clots and/or vertical layers of blood ≥1 mm thick	Thick SAH present, no IVH	Moderate disability. Requires help, but can walk unassisted.	GCS: 13–14 with neurological deficit
4	Diffuse or no subarachnoid blood, but with intracerebral or intraventricular clots	Thick SAH present, with IVH	Moderate–severe disability. Unable to walk unassisted.	GCS: 7–12
5			Severe disability. Requires constant nursing.	GCS<7
6			Dead	

[a] Intraventricular hemorrhage.

Table 2. Demographic information of patients.

Variable	All
Sex (n=642)	642 (100%)
Male	262 (40.8%)
Female	380 (59.2%)
Age (mean±SD)	54.72±13.51
Aneurysm size (mean±SD)	7.53±6.20
Aneurysm neck size (mean±SD)	3.53±2.05
GCS (mean±SD)	13.08±2.94
Aneurysm type (n=572)	
Saccular	572 (89.1%)
Large saccular	13 (2.0%)
Giant saccular	10 (1.6%)
Dissecting saccular	1 (0.2%)
Dissecting	11 (1.7%)
Desiccant	6 (0.9%)
Serpentine	1 (0.2)
Pseudoaneurysm	2 (0.3%)
Blister	6 (0.9%)
Giant	9 (1.4%)
Recanalized	11 (1.7%)
Aneurysm location (n=654)	
ICA	177 (27.6%)
MCA	86 (13.4)
ACoA	244 (38%)
ACoA–A1	9 (1.4%)
Vertebrobasilar	82 (12.8%)
Perical	42 (6.5%)
PCA	14 (2.2%)
Number of aneurysms (n=640)	
1	593 (92.7%)
2	41 (6.4%)
3	5 (0.8%)
4	0 (0%)
5	1 (0.2%)
Fisher (n=541)	
1	48 (7.5%)
2	206 (32.1%)
3	255 (39.7%)
4	32 (5%)
M Fisher (n=495)	
1	214 (33.3%)
2	17 (2.6%)
3	175 (27.3%)
4	89 (13.9%)
MRS (n=602)	
0	50 (8.3%)
1	394 (65.4%)
2	49 (8.1%)
3	34 (5.6%)
4	21 (3.5%)
5	5 (0.8%)
6	49 (8.1%)
WFNS	
1	342 (53.3%)
2	96 (15%)
3	21 (3.3%)
4	136 (21.2%)
5	38 (5.9)
Adverse events following surgical treatment	
None	570 (89.1%)
Ischemia	1 (0.2%)
Coil migration	2 (0.3%)
Perforation at coiling	1 (0.2%)
PCA occlusion	1 (0.2%)
Perforation	1 (0.2%)
Hydrocephalus	99 (16%)
Infection	19 (3.1%)
Mass Effect	2 (0.3%)
Recurrent hemorrhage	3 (0.5%)
SAH	118 (18.4%)
Death	41 (6.4%)

Quantitative data were presented as mean±SD or median (interquartile range), and compared using Mann-Whitney U and student-t tests. A *p*-value<0.05 was considered statistically significant.

Results

The present study involved 642 patients with non-traumatic SAH, including 380 (59.2%) females and 262 (40.8%) males. The mean age of the patients was 54.72±13.51. A total of 595 patients (92.7%) had only one aneurysm, while 6.4% and 0.2% had 2 and 5 aneurysms, respectively. The demographic information of the participants is presented in Table 2. When categorized based on the WFNS classification, the majority of participants were assigned to class 1 (53.3%) and class 4 (21.2%), respectively. However, when categorized based on the MRS classification, 65.4% of all participants fell into class 1. Table 2 shows the distribution of patients in the categories of these classification systems.

Saccular aneurysms were the most predominant type of aneurysm among the participants (89.1%). The least prevalent types of aneurysms were serpentine (0.2%) and dissecting saccular (0.2%) aneurysms. The most frequently involved arterial branches were the anterior communicating artery (ACoA; 38%), internal carotid artery (ICA; 27.6%), and middle cerebral artery (13.4%), while the least commonly involved arteries included the A1 segment of ACoA (1.4%) and posterior cerebral artery (PCA; 2.2%) (Table 3).

In terms of adverse events and complications, 89.1% of patients did not develop any sort of complications following surgical intervention. Recurrent SAH was the most frequently reported complication (18.4%), followed by hydrocephalus (16%), and death (6.4%). The prevalence of other complications is presented in Table 3.

Statistical analysis revealed a significant correlation between sex and the location of aneurysm, particularly ACoA, and ICA. About 33.4% of female patients had ICA aneurysm, while only 19.1% of males were reported to have the same condition ($p<0.0001$). In the case of ACoA, 46.6% of male participants had an aneurysm at this branch, which was significantly higher than the 32.1% of females who had the same condition ($p<0.0001$). Although not as significant as the two former arteries, the A1 segment of ACoA was also significantly associated with sex, with a higher proportion of male patients inclined to have an aneurysm in this branch ($p=0.02$). The relationship between sex and aneurysm location is presented in Table 4.

A significant correlation was found between age and sex. The mean age of female patients was significantly higher than males ($p<0.0001$). Patients with ICA aneurysms had a significantly lower mean age than those who did not have an aneurysm at this arterial branch. The information regarding the correlation between age, sex, and aneurysm location is summarized in Table 4.

Discussion

The present study investigated demographics and clinical features of 642 patients with non-traumatic SAH, with a mean age of 54.72±13.51, and sex distribution of 59.2% and 40.8% for females and males, respectively. According to the Fisher scale, 7.5%, 32.1%, 39.7%, and 5% of patients were categorized as classes 1-4, respectively. 89.1% of patients had no complications following surgical intervention. As previous research reported non-

Table 3. The statistical association between sex and the location of aneurysm

Aneurysm location	Patients		*p*-value[a]
	Male	Female	
ICA	50 (19.1%)	127 (33.4%)	<0.0001
MCA	34 (13%)	52 (13.7%)	0.79
ACoA	122 (46.6%)	122 (32.1%)	<0.0001
ACoA–A1	7 (2.7%)	2 (0.5%)	0.02
Vertberobasilar	31 (11.9%)	51 (13.4%)	0.56
Perical	16 (6.1%)	26 (6.8%)	0.71
PCA	7 (2.7%)	7 (1.8%)	0.47

[a]Chi-squared test was used for statistical analysis.

Table 4. Statistical associations among age, aneurysm size, aneurysm neck size, GCS, and MRS

Variables	Patients (mean±SD)		*p*-value[a]
	Male	Female	
Age	52.25±13.68	56.42±13.13	<0.0001
Aneurysm size (mm)	7.81±7.33	7.34±5.27	0.35
Aneurysm neck size (mm)	3.47±1.95	3.56±2.12	0.61
GCS	12.95±3.00	13.19±2.98	0.37
MRS	1.63±1.55	1.68±1.56	0.69

[a]Independent T-test was used for statistical analysis.

traumatic SAH tended to occur most frequently in individuals between the ages of 40 and 60, the present study found a comparable age group [14]. This age group was considered to be at higher risk for developing vascular abnormalities, such as aneurysms, which are a common cause of non-traumatic SAH. However, it is important to note that SAH can occur at any age, including in children and the elderly.

Moreover, previous studies found that the incidence of non-traumatic SAH increased with age, with older individuals being more prone to experience this type of hemorrhage. This could be attributed to age-related changes in blood vessels and increased prevalence of risk factors such as hypertension and smoking.

A recent study by Lissak *et al.,* on non-traumatic SAH, reported a mean age of 57 for patients, of whom 73% were female [15]. There is evidence that non-traumatic SAH is more common in women than in men [11]. The reasons for this sex difference are unclear, but hormonal factors may play a role in increasing the risk of vascular abnormalities in women.

The highest incidence rates for complications were 61% and 49% for hydrocephalus and delayed cerebral ischemia, respectively [15], which was in contrast with the findings of the present study, in which the most frequent complication was a recurrence of SAH (18.4%), followed by hydrocephalus (16%), with an incidence rate of only 0.2% for ischemia. One major reason for the significantly higher rate of ischemia in the previous study could be the long duration of patient follow-up, which provided enough time for the development of delayed cerebral ischemia. Moreover, based on MRS classification, the majority of participants (71%), in the study by Lissak *et al.,* were categorized as class 4-6. In contrast, a great proportion of our participants were categorized as class 0-3, suggesting that the overall clinical conditions of patients in the present study were fairer than those of the previous investigation. Despite these differences, both studies suggested that MRS classification was not correlated with sex ratio, nor was it associated with nosocomial complications such as Clostridium difficile and urinary tract infections, pneumonia, and sepsis.

Bogossian *et al.* conducted a study on SAH and reported a 57% mortality rate for a total of 353 patients in the WFNS classes 4 and 5. The majority of these deaths (nearly 80%) were observed with patients in WFNS class 5 (corresponding to Fisher classes 3-4), who generally required more rigorous treatment. This investigation concluded that the occurrence of hydrocephalus was correlated with a lower mortality rate [16]. The WFNS grading system is routinely used to determine the severity of SAH and predict the patient's outcome. It is important to note that these mortality rates are estimated and may vary depending on various factors, such as age, comorbidities, and treatment received. Early detection and appropriate management of SAH are critical in improving patient outcomes and reducing mortality rates.

Fragata *et al.* investigated the SAH and reported a mean age of 60 and a prevalence of 63% for female patients. 54% of all patients were categorized as WFNS class 1, indicating an overall fair clinical condition upon admission. Similar to our findings, they found no significant associations between sex and MRS classification [17].

Konczalla *et al.* conducted a study on 125 patients with traumatic SAH and reported a mean age of 56. Based on this investigation, 85% of patients were deemed to be in fair clinical condition (WFNS classes 1-3) when they were admitted to the hospital. Therapeutic interventions resulted in desirable outcomes in 83% of patients (MRS classes 0-2), with hydrocephalus as a secondary complication reported in 29% of participants, and death in 10% of patients. While there was no meaningful correlation between age and MRS classification, Konczalla *et al.* concluded that the clinical condition of patients at the time of admission, based on WFNS classification, was the only independent variable associated with the clinical outcome [18].

Lin *et al.,* published the findings of their investigation on 627 non-traumatic SAH patients in Taiwan, highlighting a mean age of 55 and a prevalence rate of 8.82 in every one million individuals, while refuting a significant association between age and SAH. Nevertheless, the study concluded that the age of onset in women was significantly higher than in men, which was in line with the findings of the present study. They also reported a mortality rate of 13% [19], which was roughly two times higher than what we observed with our patients.

Morita *et al.* investigated the epidemiology of SAH in a cohort of 283 Japanese patients, reporting a mean age of 62, and an average diameter of 5.7 mm for aneurysms located in different parts of the cranium. According to their findings, the prevalence of aneurysm was 36.2% for the middle cerebral artery (MCA), 18.6% for the internal carotid artery (ICA), and 15.5% for the anterior communicating artery (ACoA) [20]. On the contrary, the findings of the present study indicated that the prevalence of aneurysm was 38% for the ACoA, 27.6% for ICA, and 13.4% for MCA. It seems that there are several reasons for variances in aneurysm site studies; heterogeneity in patient population characteristics such as age, sex, comorbidities, and risk factors might also influence the distribution of aneurysm locations in SAH. Studies with diverse patient populations may reveal different patterns of aneurysm locations.

One of the strengths of our study was the examination of a large number of patients, who were admitted to a referral hospital in the East of Iran over a 10-year period. The lack of follow-up of patients for 30 days or longer was beyond the limitations of this study.

Similar to any other research, the present study had several limitations. The first one was that the patient's health records contained missing information. Nonetheless, we made an effort to make up for this problem by enrolling as many qualified patients as we could. We anticipate that the findings of the present will be complemented in the future by further clinical research.

In conclusion, the present study indicated a significant correlation between sex and the aneurysms occurring at ICA and ACoA. Additionally, as the mean age of female patients was significantly higher than that of male patients, this research revealed a statistically significant correlation between the patient's sex and age. This finding warrants a more conservative approach toward male patients who present with headaches at younger ages.

Declaration

Ethics approval and consent to participate. This study was approved by the Research Ethics Committee of Mashhad University of Medical Sciences (code: IR.MUMS.MEDICAL.REC.1398.085). All of the data from this study is available and will be provided upon request for scientific purposes.

Conflict of Interest: None.

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Author's Contribution: EVM and SRAK Conceptualization, Methodology, MZ, and MSK Data curation, Software, and Writing- Original draft preparation. HBV and MTD Visualization, Investigation, ZA, MSK and EVM, Supervision, SRAK, BRK Validation, and HBV resources, all authors finalized the manuscript.

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