ORIGINAL ARTICLE

Prevalence of Hemorrhagic Stroke Subtypes, Etiological Causes and Its Association with Various Stroke Related Risk Factors: An Observational Study

Kanika Suri[1], Puneet Rijhwani[2], Somesh Gupta[3], Mukesh Jain[4], Sumeet Garg[5], Pardeep Agarwal[6], Mukesh Sarna[7], Manish R Pahadia[8]

Received on: 17 March 2023; *Accepted on:* 12 April 2023; *Published on:* 16 September 2023

Abstract

Background: Hemorrhagic stroke (HS) is a significant cause of mortality and morbidity worldwide. This observational study aimed to determine the prevalence of HS subtypes and their association with various stroke-related risk factors.

Materials and methods: We conducted a prospective analysis of 38 patients diagnosed with HS at a tertiary health center in Rajasthan, India. We analyzed data related to demographic variables, clinical features, imaging findings, and risk factors related to HS.

Result: In our study, the male-to-female ratio was 5.3:1. The most common age-group affected by HS was 60–69 years. The incidence of intraparenchymal bleeding was 81.6%, and subarachnoid was 18.4%. Basal ganglia (50%) was the most frequent site of HS. Hypertension (HTN) was the most commonly associated risk-factor associated with HS. Chi-square analysis observed a significant association between HS and HTN ($p = 0.041$) and cardiovascular disease (CVD) ($p = 0.005$).

Conclusion: In our study, we observed a higher prevalence of HS in males and older adults. HTN was the most commonly associated modifiable risk-factor. Prompt identification and control of risk factors, particularly HTN, may help in the prevention and management of HS. More studies are needed to confirm the findings and explore the underlying mechanisms.

Keywords: Bleed, Hemorrhage, Hemorrhagic stroke, Hypertension, Stroke.

Journal of Mahatma Gandhi University of Medical Sciences and Technology (2022): 10.5005/jp-journals-10057-0217

Introduction

World Health Organization (WHO) described stroke "as promptly evolving clinical signs of focal, at times global disturbances of cortical function lasting for >24 hours or causing death with no obvious reason other than vascular origin."[1] In their 2013 updated definition, American Heart Association/American Stroke Association defined intracerebral hemorrhage (ICH) as "promptly evolving clinical signs of neurological dysfunction attributable to a focal collection of blood within the brain parenchyma or ventricular system that is not caused by trauma." It further defined stroke caused by subarachnoid hemorrhage (SAH) as "rapidly developing signs of neurological dysfunction and/or headache because of bleeding into the subarachnoid space which is not caused by trauma."[2]

Worldwide, 15 million people suffer from stroke every year, according to the WHO. The third most common cause of disability is stroke.[3] Occurrence of hemorrhage is higher in Asians (15–40%) contrasted with 15–20% in the developed nations.[3] Based on neuroimaging results, studies have shown that stroke subtypes and cerebral infarction to hemorrhage proportions of 1.86:1–2.21:14.[4] As a result, the ratio of infarction to hemorrhage in the Indian subcontinent is significantly higher than in Western nations, where it is 5:1. Only 50–60% of adequate neuroimaging was available in these studies.

Hemorrhagic stroke (HS) is due to bleeding from any brain-supplying blood vessel. SAH, typically caused by a ruptured aneurysm, can also lead to a stroke. Usually, it is more severe and linked to increased early mortality. The most frequent cause of HS is HTN. Although the rate and mortality of stroke due to ICH have gradually lowered, HS actually represents 10–20% of stroke patients.[5] The worldwide burden of HS is continuously expanding. The distribution of risk factors and their impact on HS might fluctuate by geographic region and social factors. This review concentrated on the clinical profile and different risk factors impacting the incidence of HS in and around Rajasthan.

[1–8]Department of General Medicine, Mahatma Gandhi Medical College & Hospital, Jaipur, Rajasthan, India

Corresponding Author: Kanika Suri, Department of General Medicine, Mahatma Gandhi Medical College & Hospital, Jaipur, Rajasthan, India, Phone: +91 9871600996, e-mail: kanikasuri_13@hotmail.com

How to cite this article: Suri K, Rijhwani P, Gupta S, *et al.* Prevalence of Hemorrhagic Stroke Subtypes, Etiological Causes and Its Association with Various Stroke Related Risk Factors: An Observational Study. J Mahatma Gandhi Univ Med Sci Tech 2022;7(3):78–83.

Source of support: Nil

Conflict of interest: None

Materials and Methods

It is a prospective cross-sectional study. Data were collected from patients diagnosed with acute HS admitted to the Department of Medicine at a tertiary care center in Rajasthan, from January 2021 to 2022. Both genders were incorporated into our study.

Inclusion Criteria

Age: Patients with the age of 18 years and above.

- Sex:
  - Male.
  - Female.
- All patients were diagnosed with acute HS.

Exclusion Criteria

- Patients age <18 years.
- Patients diagnosed as transient ischemic attacks (TIAs).
- Patients diagnosed with ischemic stroke.
- Patients presenting as stroke mimics—(tumor, subdural hematoma, demyelination, and postictal deficit).
- Patients with encephalopathies (metabolic and drug).
- Sinus venous thrombosis.
- Patients are not willing to give consent.
- Stroke patients without appropriate imaging studies to characterize the stroke subtype.

A total of 38 patients were selected as potential study participants. Individuals >18 years who presented within the initial 24 hours of the onset of symptom and had a magnetic resonance imaging (MRI) or computed tomography (CT) scan that confirmed a diagnosis of HS was selected. Those who were willing to participate were asked to sign a written consent form. According to the hospital's stroke management protocol, the doctor decides how to treat each patient.

Stroke is diagnosed as—"promptly evolving clinical signs of focal (or global) disturbance of cerebral function, lasting >24 hours or causing death, with no obvious reason other than that of vascular origin." Ischemic stroke and HS are two types of strokes. Excluded from the study were patients who had only experienced a TIA.

Diagnosis of HS—HS is identified by imaging including a CT scan or MRI brain. HS is subdivided into:

- Intraparenchymal hemorrhage.
- Subarachnoid hemorrhage (SAH).

Data Collection

Included were baseline vital signs, demographic data (age, gender, socioeconomic status, and body mass index), a history of HTN, coronary heart disease, vasculitis, dyslipidemia, atrial fibrillation, and other cardio-metabolic risk factors like alcohol consumption and smoking, a family history of stroke, a history of thrombolytic therapy and/or surgical procedures, and dietary information. In addition, reports of the diagnosis from a two-dimensional echocardiogram, a CT/MRI of the brain, and a CT angiography of the brain were gathered to support the diagnosis.

Table 1: Gender and age-group distribution in the study population as well as their association with hemorrhagic stroke

	Hemorrhagic stroke (N = 38)	*p-value*
Gender		
Male	32 (84.2)	0.010
Female	6 (15.8)	
Age-group		
18–39 years	1 (2.6)	0.008
40–49 years	3 (7.9)	
50–59 years	11 (28.9)	
60–69 years	16 (42.2)	
≥70 years	7 (18.4)	
Mean ± SD	62.9 ± 2.8	0.029

Statistical Analysis

Microsoft Excel was used to collect and tabulate the data. Data was introduced as the mean ± standard deviation (SD) or the median, depending on their distribution. The distinctions in quantitative factors between subgroups were surveyed utilizing an unpaired *t*-test. The groups were compared using the nonparametric Mann–Whitney test. Analysis of variance was used to determine the variables. The difference between the groups in categorical variables was evaluated using the Chi-squared test.

Observation and Results

The male-to-female ratio was 5.3:1 (N = 38, male-32; female-6). While analyzing gender status, it was observed that the majority were males (84.2%).

While analyzing age distribution, it was observed that the majority in the HS group belonged to the 60–69 class interval (42.2%) with a mean age of 62.9 (SD-2.8) years (p = 0.029). The statistical association between HS and increasing age was found to be significant (p = 0.008) (Table 1).

In this study, the commonest clinical feature was hemiplegia/hemiparesis (87.6%); among those left-sided weakness was more common (54.3%). Speech disturbances were found in 43.8% of patients, out of which 85.9% of patients had dysarthria, and 14.1% of patients had motor aphasia. Cranial nerve involvement in the present study was 10%.

Hemorrhagic stroke (HS) was further subdivided into intraparenchymal and subarachnoid according to the site of bleeding. The incidence of intraparenchymal bleeding was 81.6% and subarachnoid was 18.4%.

In the current study, basal ganglia 19 (50.0%) was the most frequent site of bleeding in HS, followed by thalamus 9 (23.7%), and cerebellum 3(7.9%). Subarachnoid bleeding was observed in 13.2% of cases. (Table 2).

In the current study, the risk factors of HS were divided into nonmodifiable and modifiable risk factors. In the intraparenchymal group, the mean age was 64.4 ± 2.6 years, while 84.8% were male patients included in the current study. Around 15.2% of patients had a significant family history of stroke, and 6.1% of patients had a prior history of stroke/TIA in the intraparenchymal group.

In a subarachnoid group of stroke patients, the mean age was 61.5 ± 3.0 years while 80% were male patients included in the current study. No patients had a family history of stroke and prior history of stroke/TIA in this group.

In the intraparenchymal group patients of stroke patients, major modifiable risk factors were HTN (84.8%), CVD (45.5%), and

Table 2: Site of localization of bleeding in hemorrhagic stroke (N = 38)

Site of bleeding	*No.*	*Percentage*
Basal ganglia	19	50.0
Thalamus	9	23.7
SAH	5	13.2
Cerebellum	3	7.9
Lobar	1	2.6
Pons	1	2.6

diabetes mellitus (DM) (24.2). Other risk factors were obesity (24.2%) and tobacco chewing (30.3%).

In subarachnoid group patients of stroke patients, major modifiable risk factors were (40%), and HTN alcohol abuse (60%). One patient (20%) had CVD in stroke patients. (Tables 3 and 4).

Out of the 38 individuals with HS, 30 (78.9%) were found to have HTN as a potential cause of their condition. One patient (3.03%) had a history of bleeding disorder while two patients (6.06%) had a history of anticoagulant usage. No individuals were found to have cerebral amyloid angiopathy (CAA) or arteriovenous malformations (AVM) as potential causes of their condition, and none were under drug abuse (Table 5).

Out of the five individuals of SAH, four patients (80.0%) had aneurysms located in the anterior communicating artery (ACA), one patient (20.0%) had aneurysms in the middle cerebral artery (MCA), and none had aneurysms in the vertebral artery, basilar artery or posterior communicating artery (PCA) (Table 6).

The Chi-squared test was used to analyze possible associations between comorbid risk factors and stroke subtypes. It concluded that compared to other comorbid risk factors, HTN ($p = 0.041$) CVD ($p = 0.005$), and tobacco chewing ($p = 0.204$) were significantly prevalent among HS patients.

Table 3: Risk factors according to hemorrhagic stroke subtypes

Risk factors	*Intraparenchymal (N = 33)*	*Subarachnoid (N = 5)*
Nonmodifiable risk factors		
Age	64.4 ± 2.6	61.5 ± 3.0
Sex (male)	28 (84.8)	4 (80.0)
Prior stroke/TIA	2 (6.1)	0 (0.0)
Family history of stroke	5 (15.2)	0 (0.0)
Modifiable risk factors		
Hypertension	28 (84.8)	2 (40.0)
DM	8 (24.2)	0 (0.0)
Smoking	2 (6.1)	0 (0.0)
Dyslipidemia	2 (6.1)	0 (0.0)
CVD	15 (45.5)	1 (20.0)
Alcohol abuse	1 (3.0)	3 (60.0)
Tobacco chewing	10 (30.3)	0 (0.0)
Obesity	8 (24.2)	0 (0.0)
Drug abuse	0 (0.0)	0 (0.0)
Obstructive sleep apnea	2 (6.1)	0 (0.0)

Table 4: Association of risk factors distribution in HS patients

Risk factors	*Hemorrhagic stroke (N = 38)*	*p-value*
Hypertension	30 (78.9)	0.041
DM	8 (21.1)	0.022
Smoking	2 (5.3)	0.002
Dyslipidemia	2 (5.3)	0.000
CVD	16 (42.1)	0.005
Alcohol consumption	4 (10.5)	0.262
Prior stroke/TIA	2 (5.3)	0.018
Family history of stroke	5 (13.2)	0.247
Tobacco chewing	10 (26.3)	0.204
Obesity	8 (21.1)	0.339
Drug abuse	0 (0.0)	0.150
Obstructive sleep apnea	2 (5.3)	0.593

Discussion

The present study effectively analyzes the risk factors and causes of acute HS in the Indian setting and provides a distribution of the various etiological HS subtypes in a hospital-based sample. During the review period, we inspected 38 patients who had a clinical and radiologically affirmed diagnosis of HS tentatively.

In cases of intra-parenchymal bleeding, the median age was 64.4 ± 2.6 years, while in cases of subarachnoid bleeding, it was 61.5 ± 3 years, with ages ranging from 18 to 76 years. It was clear that the strokes were most pervasive in the age-gathering of 60–69 years. This study's findings were comparable to those of other Indian studies.[6] Age is a nonmodifiable factor that has been shown to increase the risk of stroke with age. The Neurological Society of India reported that, like ours, the age-specific incidence of stroke was higher in the 60s and 70s.[7]

The male:female proportion was 5.3:1; In general, there was a male preponderance, which was similar to what was found in other studies.[8] Moreover, a meta-analysis from 19 countries reported that the incidence (33%) and prevalence (41%) of HS were more noteworthy in men than women. The fact that men are more likely to seek medical attention may also be a factor in the lower percentage of women.

In our study, the most frequent site of HS was observed to be the basal ganglia (50%) followed by the thalamus (23.7%). Chen et al. in their review expressed that the common sites of HS were the basal ganglia (50%), cerebral lobes (10–20%), pons and the brain stem (10–20%), thalamus (15%), and cerebellum (10%).[9] Lee et al. also reported that intraventricular hemorrhage was more common in the thalamus and basal ganglia.[10] In our study, ACA (80%) was the most common site of aneurysmal rupture, followed by the MCA (20%). According to the International Study of Unruptured Intracranial Aneurysms, which included 4,060 patients with unruptured intracranial aneurysms, the majority of aneurysms occur in the anterior circulation of the circle of Willis, whereas only 12% of intracranial aneurysms occur in the posterior circulation of the vertebral and basilar systems. Likewise, the

Table 5: Distribution of etiological causes of ICH

Etiology	*ICH (N = 33)*
Hypertension	30 (90.9)
CAA	0 (0.0)
Arteriovenous malformation	0 (0.0)
Bleeding disorders	1 (3.03)
Illicit drug abuse	0 (0.0)
Antiplatelets/antithrombotics	2 (6.06)

Table 6: Site of aneurysmal rupture in SAH

Site of aneurysms	*Number = 5*
ACA	4 (80.0)
MCA	1 (20.0)
PCA	0 (0.0)
Basilar artery	0 (0.0)
Vertebral artery	0 (0.0)

latest Japanese cohort study showed the comparative frequency of rupture for anterior and posterior circulations. In addition, the authors discovered that ACA aneurysms had a higher rate of rupture than PCA aneurysms.

According to Siddique et al.[11] and Baidya et al.,[12] hemiplegia was the most common presentation of HS in India (80%), followed by dysarthria (60%), and aphasia (59%), respectively. Hemiparesis and hemiplegia were the most common presentations of stroke (87.6%). Patients with dysarthria/aphasia had fewer speech defects (43. 8%) in our study. This distinction could be attributed to the type of study, such as the current forward cohort study or the backward cohort study.

The risk factors for HS can be arranged into modifiable (HTN, diabetes, cardiovascular infection, dyslipidemia smoking, and customary liquor consumption) and nonmodifiable elements (counting age, orientation, and earlier history of stroke).

In general, the prevalence of HS has been linked to a number of risk factors, including smoking, alcohol consumption, diabetes, HTN, dyslipidemia, and DM. It is now well-known that high blood pressure (BP) is a significant risk-factor for HS.

Although HTN was found to be the most common risk-factor for HS (78.9%), the Chi-squared test found that these findings were statistically significant (P0.05). 64% of stroke patients in Gorgan, according to Hosaini and Bazrafshan;[13] had high BP, regardless of the type of stroke. Law et al.'s study of clinical trial meta-analysis (2009) expressed that the frequency of HS was lessened by 41% when both systolic and diastolic pulses were reduced.[14] It appears to be that antihypertensive treatment along with modifications in lifestyle can diminish the risk of HS and its recurrence. A review has revealed that inadequate BP control has a more prominent likelihood of ICH relapse than patients with ICH who have a history of admission of antiplatelet drugs, the incidence of ICH relapse and volume of hemorrhage didn't increase.[15]

This study entails a significant connection between diabetes and HS. According to our findings, 21% of all HS patients were diabetic. Diabetes management may also reduce mortality and prevent both primary and secondary HS. Variable data exist for diabetes to be a risk-factor for ICH. Pooled investigations of Atherosclerosis Risk in Communities and Cardiovascular Health Studies disclosed an age-adjusted relative rate of 1.11 for people who have diabetes and ICH.[16] Men in the Honolulu Heart Program and the Framingham Study had similar rates of bleeding, but only those with diabetes were at an increased risk for ICH in the Framingham group (relative risk, 3.1).[17]

Dyslipidemia was a significant risk factor that was observed in 5. 3% of the HS patients, which was consistent with previous findings that were reported by Tziomalos et al.[18] In-hospital mortality rate is almost twice as high in patients who do not have diabetes compared to those who do[19] and Sarti et al.[20] A total serum cholesterol level of 4.62 mmol/L (178 mg/dL) was associated with a significantly greater risk for ICH in men aged 65 years or older (relative risk, 2.7; Kaiser Permanente Study).[21] This relationship between total serum cholesterol and low-density lipoprotein cholesterol and hemorrhages is consistently reported[22] (95% confidence interval, 1.4–5.0). Patients with lower total serum cholesterol levels have been found to have a higher rate of in-hospital mortality within the first 48 hours of admission.

A risk-factor for HS includes heart disease. People with coronary course sickness or ongoing cardiovascular breakdown are 2–4 times as prone to have HS.[23] Examinations showed that HS accounted for 20–32%, with extracranial (25–26%) and intracranial (30%) carotid diseases.[24] In this study, cardiac diseases accounted for 42.1% of HS patients.

In India, the rising prevalence of tobacco use is a major health concern. In addition, a rise in noncommunicable diseases can be attributed to the lifestyle changes brought about by urbanization and industrialization. Two HS patients, or 5.3%, in our study, were smokers. In accordance with this study, Donnan et al.[25] discovered that smoking was a significant risk-factor for SAH. Numerous studies have identified smoking as a risk-factor for cerebral hemorrhage. This connection to SAH is well established, particularly among Asians.[26] However, smoking is not as strongly associated with primary intracranial bleeding. Similar findings were obtained in studies conducted in Australia, Norway, and Poland.[27] Excessive alcohol consumption has been identified as a risk-factor for HS. In our study, 4.5% of the patients had previously consumed alcohol. It is thought that alcohol has an effect on the coagulation pathway and the integrity of the cerebral vessels.[28]

Drug abusers have a higher risk of HS. It is a frequent cause of ICH in young adults in areas with a high prevalence of illicit drug use. Psychomotor stimulants like cocaine and amphetamine, are more frequently linked to HS.[29] The case reports of amphetamine use and ICH are generally seen in the youth.[30] A 1-year long case series of all deadly ICH cases inspected by the Connecticut office of the Main Clinical Inspector reported that 59% were related to cocaine misuse.[31]

The current study found a significant link between smoking and HS. In our study, 26. 3% of HS patients smoked. Nicotine starts with many different pathological mechanisms like platelet activation, endothelial dysfunction, atherogenesis, sympathoadrenal activation, arrhythmia, relative insulin resistance, and dyslipidemia, all of this prompt vascular damage and causes CVD including stroke.[32] Consumption of snuff was linked to an increased risk of SAH in one Swedish study.[33]

A condition known as CAA is responsible for around 12–15% of all cerebral hemorrhages in elderly people. Amyloid-β precursor protein–associated CAA is the most common type of ischemic and HS. CAA was seen during post-mortem in over half of individuals aged 90 years or more.[34] Clinical series revealed that CAA-related ICH may specially influence the frontal lobe, despite the fact that posteriorly found hemorrhages in the brain hemisphere are accepted to be common.[35] Amyloid angiopathy is additionally connected with repetitive ICH and warfarin-related bleeds.[36]

Oral anticoagulation (OAC) increases the risk for ICH. Patients receiving OAC have a 7–10 fold increased risk of ICH compared to those receiving no treatment, according to numerous studies. Two of the patients in our study had previously taken anticoagulants. Anticoagulant medications may be linked to between 10 and 12% of all ICH. OAC-related ICH has a mortality rate of approximately 50%. In contrast to spontaneous ICH, the initial event is followed by 12–24 hours of bleeding.[37]

Anticoagulants have a greater impact on ICH than antiplatelet medications do. According to, Gorelick and Weisman patients taking aspirin for primary prevention of myocardial infarction have a risk of 0.2 events per 1,000 patient in years[38] Several studies have shown that antiplatelet use is associated with worse outcomes. Biffi et al. have discovered that antiplatelet therapy may increase the likelihood of ICH recurrence in lobar hemorrhage patients.[39]

Arteriovenous malformations (AVMs) are a relatively rare condition, with an estimated prevalence of 0.1–0.5% in the general population. The most common presentation of AVMs is HS, which occurs in approximately 50% of cases. AVMs can cause HS by

rupturing and bleeding into the brain tissue, leading to neurological deficits and potentially life-threatening complications.

Bleeding disorders can build the risk of HS by debilitating the body's capacity to form clots and keep up with hemostasis. ICH and SAH are more likely to happen to people who have bleeding disorders. Hemophilia, specifically, is related to a higher risk of ICH, with a reported incidence of up to 5% in severe hemophilia patients. Patients with bleeding disorders who have an HS may also be at higher risk of poor outcomes and are more likely to die or become disabled. In the current review, one patient had idiopathic thrombocytopenic purpura. Around 23.7% with ICH died. Similar outcomes were also observed in other studies.

Conclusion

According to the study, males and people between the ages of 60 and 69 are more likely to suffer from HS. The most well-known clinical component was hemiplegia/hemiparesis, with left-sided weakness being more frequent. The most prevalent subtype of HS was intraparenchymal bleeding, with basal ganglia bleeding being the most common. HTN, CVD, and alcohol were the major modifiable risk factors related to HS.

The study sheds light on the prevalence of HS subtypes and their relationship to various risk factors for stroke in the Rajasthani population. Understanding the disease's burden and developing appropriate preventative measures depend on such studies. The development of effective interventions to reduce the prevalence of HS in the general population can also benefit from the identification of modifiable risk factors. To confirm the findings of this study and gain a deeper comprehension of the disease, additional studies with larger sample sizes and multicenter settings are required.

Orcid

Puneet Rijhwani https://orcid.org/0000-0002-9454-736X

References

1. Warlow CP. Epidemiology of stroke. Lancet 1998;352(3):1–4. DOI: 10.1016/S0140-6736(98)90086-1
2. Sacco RL, Kasner SE, Broderick JP, et al. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2013;44(7):2064–2089. DOI: 10.1161/STR.0b013e318296aeca
3. Hisham NF, Bayraktutan U. Epidemiology, pathophysiology, and treatment of hypertension in ischaemic stroke patients. J Stroke Cerebrovasc Dis 2013;22(7):e4–e14. DOI: 10.1016/j.jstrokecerebrovasdis.2012.05.001
4. Banerjee TK, Mukherjee CS, Sarkhel A. Stroke in the urban population of Calcutta: an epidemiological study. Neuroepidemiology 2001;20(3):201–207. DOI: 10.1159/000054788
5. D'Souza S. Aneurysmal subarachnoid hemorrhage. J Neurosurg Anesthesiol 2015;27(3):222–240. DOI: 10.1097/ANA.0000000000000130
6. Department of Health. Research. Annual report 2013–2014.
7. WHO. The global burden of disease: 2004 update. Geneva, Switzerland: WHO; 2008.
8. Renjen PN, Beg MA, Ahmad K. Epidemiological study of incidence and risk factors of Ischemic stroke subtypes according to Trial of ORG 10172 in acute stroke treatment criteria: a 3 years, hospital-based study. Int J Med Public Health 2015;5(1):50–54. DOI: 10.4103/2230-8598.151258
9. Chen R, Ovbiagele B, Feng W. Diabetes and stroke: epidemiology, pathophysiology, pharmaceuticals and outcomes. Am J Med Sci 2016;351(4):380–386. DOI: 10.1016/j.amjms.2016.01.011
10. Lee SH, Park KJ, Kang SH, et al. Prognostic factors of clinical outcomes in patients with spontaneous thalamic hemorrhage. Med Sci Monit 2015;21:2638–2646. DOI: 10.12659/MSM.894132
11. Siddique A, Nur Z, Mahbub S, et al. Clinical presentation and epidemiology of stroke: a study of 100 cases. J Med 2009;10(2):86. DOI: 10.3329/jom.v10i2.2820
12. Baidya OP, Chaudhuri S, Devi KG. Clinico-epidemiological study of acute ischemic stroke in a tertiary hospital of northeastern state of India. Int J Biomed Adv Res 2013;4(9):661. DOI: 10.7439/ijbar.v4i9.486
13. Hosaini SA, Bazrafshan H. A statistical study on the role of high-risk factors in the incidence of CVA. J Univ Med Sci 2001;3(2):76–80.
14. Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. BMJ 2009;338:b1665. DOI: 10.1136/bmj.b1665
15. Taylor BC, Wilt TJ, Welch HG. Impact of diastolic and systolic blood pressure on mortality: implications for the definition of "normal". J Gen Intern Med 2011;26(7):685–690. DOI: 10.1007/s11606-011-1660-6
16. Sturgeon JD, Folsom AR, Longstreth WT Jr, et al. Risk factors for intracerebral hemorrhage in a pooled prospective study. Stroke 2007;38(10):2718–2725. DOI: 10.1161/STROKEAHA.107.487090
17. Rodriguez BL, D'Agostino R, Abbott RD, et al. Risk of hospitalized stroke in men enrolled in the Honolulu heart program and the Framingham study: a comparison of incidence and risk factor effects. Stroke 2002;33(1):230–236. DOI: 10.1161/hs0102.101081
18. Tziomalos K, Athyros VG, Karagiannis A, et al. Dyslipidemia as a risk factor for ischemic stroke. Curr Top Med Chem 2009;9(14):1291–1297. DOI: 10.2174/156802609789869628
19. Arboix A, Massons J, García-Eroles L, et al. Diabetes is an independent risk factor for inhospital mortality from acute spontaneous intracerebral hemorrhage. Diabetes Care 2000;23(10):1527–1532. DOI: 10.2337/diacare.23.10.1527
20. Sarti C, Kaarisalo M, Tuomilehto J. The relationship between cholesterol and stroke. Implications for antihyperlipidaemic therapy in older patients. Drugs Aging 2000;17(1):33–51. DOI: 10.2165/00002512-200017010-00003
21. Roquer J, Rodríguez Campello A, Gomis M, et al. Serum lipid levels and in-hospital mortality in patients with intracerebral hemorrhage. Neurology 2005;65(8):1198–1200. DOI: 10.1212/01.wnl.0000180968.26242.4a
22. Cui R, Iso H, Toyoshima H, et al. Serum total cholesterol levels and risk of mortality from stroke and coronary heart disease in Japanese: the JACC study. Atherosclerosis 2007;194(2):415–420. DOI: 10.1016/j.atherosclerosis.2006.08.022
23. Hobeanu C, Lavallée PC, Charles H, et al. Risk of subsequent disabling or fatal stroke in patients with transient ischaemic attack or minor ischaemic stroke: an international, prospective cohort study. Lancet Neurol 2022;21(10):889–898. DOI: 10.1016/S1474-4422(22)00302-7
24. Eapen RP, Parikh JH, Patel NT. A study of clinical profile and risk factors of cerebrovascular stroke. Gujarat Med J 2009;64:48–54.
25. Donnan GA, McNeil JJ, Adena MA, et al. Smoking as a risk factor for cerebral ischaemia. Lancet 1989;2(8664):643–647. DOI: 10.1016/s0140-6736(89)90894-5
26. Feigin V, Parag V, Lawes CM, et al. Smoking and elevated blood pressure are the most important risk factors for subarachnoid hemorrhage in the Asia-Pacific region: an overview of 26 cohorts involving 306,620 participants. Stroke 2005;36(7):1360–1365. DOI: 10.1161/01.STR.0000170710.95689.41
27. Jamrozik K, Broadhurst RJ, Anderson CS, et al. The role of lifestyle factors in the etiology of stroke. A population-based case-control study in Perth, Western Australia. Stroke 1994;25(1):51–59. DOI: 10.1161/01.str.25.1.51
28. Qureshi AI, Tuhrim S, Broderick JP, et al. Spontaneous intracerebral hemorrhage. N Engl J Med 2001;344(19):1450–1460. DOI: 10.1056/NEJM200105103441907
29. Fonseca AC, Ferro JM. Drug abuse and stroke. Curr Neurol Neurosci Rep 2013;13(2):325. DOI: 10.1007/s11910-012-0325-0

30. Cahill DW, Knipp H, Mosser J. Intracranial hemorrhage with amphetamine abuse. Neurology 1981;31(8):1058–1059. DOI: 10.1212/wnl.31.8.1058-a
31. Nolte KB, Brass LM, Fletterick CF. Intracranial hemorrhage associated with cocaine abuse: a prospective autopsy study. Neurology 1996;46(5):1291–1296. DOI: 10.1212/wnl.46.5.1291
32. Benowitz NL. Cigarette smoking and cardiovascular disease: Pathophysiology and implications for treatment. Prog Cardiovasc Dis 2003;46(1):91–111. DOI: 10.1016/s0033-0620(03)00087-2
33. Koskinen LO, Blomstedt PC. Smoking and non-smoking tobacco as risk factors in subarachnoid haemorrhage. Acta Neurol Scand 2006;114(1):33–37. DOI: 10.1111/j.1600-0404.2006.00591.x
34. Kalimo H. Pathology and genetics: cerebrovascular disease. Basel (Switzerland): ISN Neuropath press; 2005. p. 95.
35. Sucker C, Hetzel GR, Grabensee B, et al. Amyloidosis and bleeding: pathophysiology, diagnosis, and therapy. Am J Kidney Dis 2006;47(6):947–955. DOI: 10.1053/j.ajkd.2006.03.036
36. Yen CC, Lo YK, Li JY, et al. Recurrent primary intracerebral hemorrhage: a hospital based study. Acta Neurol Taiwan 2007;16(2):74–80.
37. Steiner T, Rosand J, Diringer M. Intracerebral hemorrhage associated with oral anticoagulant therapy: current practices and unresolved questions. Stroke 2006;37(1):256–262. DOI: 10.1161/01.STR.0000196989.09900.f8
38. Gorelick PB, Weisman SM. Risk of hemorrhagic stroke with aspirin use: an update. Stroke 2005;36(8):1801–1807. DOI: 10.1161/01.STR.0000174189.81153.85
39. Biffi A, Halpin A, Towfighi A, et al. Aspirin and recurrent intracerebral hemorrhage in cerebral amyloid angiopathy. Neurology 2010;75(8):693–698. DOI: 10.1212/WNL.0b013e3181eee40f