

Stroke-Related Risk Factors: A Review

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ABSTRACT

Stroke (cerebrovascular accident) is the second leading cause of death and long-term disability worldwide. The major risk factors of stroke are categorized as modifiable and non-modifiable. Modifiable risk factors include hypertension, diabetes mellitus, heart disease, hyperlipidemia, obesity, and smoking. Non-modifiable risk factors include age, genetic, gender, and race. Risk factors that are specific to women including pregnancy, postpartum period, and oral contraceptives, some psychological factors such as stress and depression are linked to stroke. The burden of stroke is increasing globally. Furthermore, because stroke treatment is not satisfactory, significant effort should be focused on reducing risk factors to reduce the disease's effects. The current study will provide a better understanding of risk factors associated with stroke that may further lead to improved prevention of stroke.

Keywords: Disability, Hemorrhagic stroke, Ischemic stroke, Risk factors of stroke, Stroke
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INTRODUCTION

According to the Global Burden of Diseases study in 1990, stroke was the second leading cause of death and disability worldwide.^[1] Stroke is the “incoming epidemic of the twenty-first century,” according to the World Health Organization (WHO). Recent evidence suggests that 85% of all strokes may be preventable, hence, preventative methods are becoming more prominent in stroke care. The annual death rate from stroke is estimated to be around 5.5 million. Stroke has a high mortality rate, but it also has a high morbidity rate, resulting in up to 50% of survivors being permanently disabled.^[2] With age, the prevalence rate grows. People aged 70–79 years are 4.98 times more likely to have had a stroke than those aged 40–49 years, while people aged >80 years are 4.78 times more likely to have had a stroke than those aged 40–49 years. Men had a greater prevalence rate than women, with 3.44 and 2.41/1000, respectively.^[3] Stroke is a major public health problem that is expected to worsen in the next decades as a result of population shifts, particularly in the developing nations.^[4] A stroke affects more than 795,000 people in the United States each year. The first or new strokes account for approximately 610,000 of these. A total of 185,000 strokes occur in people who have already had a stroke, accounting for approximately one-fourth of all strokes.^[5] A systematic review of electronic databases (Ovid, PubMed, Medline, and EMBASE) including studies published between January 1990 and December 2015 showed that during the past two decades, the crude stroke prevalence in various parts of India fluctuated from 44.29 to 559/100,000 people and the cumulative incidence of stroke in India has fluctuated from 105 to 152/100,000 people/year in various sections of the country.^[6] The prevalence of stroke worldwide shows that it is a globally upcoming epidemic and it is important to take some preventive measures.

STROKE

More than 2400 years ago stroke was first characterized as apoplexy, which means “to be struck down by violence,”^[7] its true also, as stroke (cerebrovascular accident) is a striking of blood vessel or rupturing of blood vessel in the brain. The WHO definition of stroke is “rapidly developing clinical signs of focal (or global) disturbance of cerebral function,” with symptoms lasting

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24 h or longer or leading to death, with no apparent cause other than of vascular origin.^[8] The American Stroke Association recently proposed a revised definition of stroke for the 21st century that includes clinical and tissue criteria. Any objective evidence of persistent brain, spinal cord, or retinal cell death attributed to a vascular etiology based on pathological or imaging data with or without the presence of clinical symptoms is included in this definition.^[9] Stroke can be explained as the sudden death of some brain cells due to lack of oxygen when the blood flow to the brain is lost by blockage or rupture of an artery to the brain.^[3]

TYPES

Stroke is broadly categorized as ischemic and hemorrhagic.

Ischemic stroke – This is the most common type of stroke, affecting around 80% of those who have one. It occurs when a clot blocks or slows blood flow, depriving the brain of oxygen and nutrients.

Hemorrhagic stroke – It occurs when blood vessels rupture, causing leakage of blood in or around the brain.^[10]

These two major categories are further divided into subtypes:

Ischemic Stroke

Ischemic stroke is defined as an episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction with symptoms

persisting for more than 24 h, whereas a transient ischemic attack (TIA) is defined as a “transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia without acute infarction.” TIAs are commonly referred to as mini-strokes because the symptoms are only temporary (i.e., lasting from minutes to hours but <24 h).^[11]

The TOAST classification is the most widely used and includes:^[12]

1. Large-vessel atherothrombosis;
2. Cardioembolism;
3. Small-vessel disease;
4. Other determined causes;
5. Undetermined causes.

Large-vessel atherothrombosis – The formation of lipid-laden atherosclerotic plaques on the inner wall of a major arterial, which can damage both extracranial and intracranial arteries.

Cardioembolism – It happens when blood clots that may have developed within the heart break away, enter the circulation, and become trapped downstream in a cerebral artery.

Small-vessel disease – It refers to occlusive disease involving the microcirculation of the brain.

Other determined causes – It includes strokes caused by extracranial arterial dissections, non- atherosclerotic vasculopathies, hypercoagulable states, or hematologic disorders.

Undetermined causes – It refers to patients who have had a full workup for cardiac conduction or structural abnormalities, intracranial or extracranial major artery stenosis, coagulopathy, and other diseases but have been unable to find a reason.

Hemorrhagic Stroke

There are two different types of hemorrhagic stroke: Subarachnoid hemorrhage (SAH), which comprises around 5% of all strokes, and intracerebral hemorrhage (ICH), which accounts for around 10% of all strokes.

1. SAH – It is the hemorrhage into the subarachnoid space, which is the region surrounding the brain where blood vessels present between the arachnoid and pia mater, from a cerebral blood vessel, aneurysm, or vascular abnormality.
2. ICH – When a weakened blood vessel within the brain ruptures, enabling blood to leak and increase intracranial pressure, causing damage to the brain cells surrounding the blood vessel.^[11]

WARNING SIGNS AND SYMPTOMS

Clinically, a wide range of focal deficit can occur, including alterations in consciousness and sensory, motor, cognitive, perceptual, and language problems.

Five stroke warning signs established by the (American) National Institute of Neurological Disorders and Stroke (2005) are as follows:^[13]

- Numbness or weakness in the face, arms, or legs (especially on one side of the body);
- Confusion, difficulty speaking, or understanding speech;
- Vision disturbances in one or both eyes;
- Dizziness, trouble walking, loss of balance, or coordination
- Severe headache with no known cause.

FAST is a simple mnemonic that anyone can use and helps to identify the key symptoms of stroke. The FAST acronym was developed in the UK in 1998 by a group of stroke physicians, ambulance personnel, and an emergency department physician

and was designed to be an integral part of a training package for ambulance staff. These are:^[14]

F – Facial drooping

A section of the face, usually only on one side, that is, drooping and hard to move. This can be recognized by a crooked smile.

A – Arm weakness

The inability to raise one’s arm fully, or the inability to hold something or squeeze, that is, someone’s hand.

S – Speech problems

An inability or difficulty to understand or produce speech, slurred speech or having difficulty repeating even a basic sentence such as “The sky is blue.”

T – Time

Time to call 999.

If any of the symptoms above are showing, time is of the essence; call the emergency services; and go to the hospital immediately. It is also important to check the time so that you’ll know when the first symptoms appeared.

STROKE-RELATED RISK FACTORS

The risk factors of stroke are of two types: Modifiable or reversible risk factors and non-modifiable or irreversible risk factors.^[15]

Modifiable risk factors include:

1. Hypertension
2. Heart disease
3. Diabetes mellitus
4. Hyperlipidemia
5. Obesity
6. Smoking
7. Excess alcohol consumption
8. Oral contraceptive
9. Physical activity
10. Diet and nutrition

Non-modifiable risk factors include:

1. Age
2. Gender
3. Race
4. Heredity

MODIFIABLE RISK FACTORS

Hypertension

Hypertension is a condition in which the force of the blood against the artery walls is too high. Hypertension is an important risk factor for both hemorrhagic and ischemic stroke.^[16] Blood pressure (BP) values exceeding 115/75 mmHg increase the risk of stroke, and high BP accounting for 54% of stroke episodes worldwide.^[17] A drop in systolic BP of 2 mmHg was linked to a 25% reduction in stroke risk, while a reduction in diastolic BP was linked to a 50% reduction in stroke risk.^[18] BP is an important modifiable risk factor and there is evidence that controlling BP levels to <150/90 mmHg reduce the risk of stroke.^[19]

Hyperlipidemia

Hyperlipidemia is caused by a high-cholesterol diet that is consumed in excess, resulting in elevated blood lipid levels. High cholesterol levels (>7.0 mmol/L) have been linked to

an increased risk of stroke.^[20] Hyperlipidemia contributes to atherosclerosis. Artherosclerosis is caused by an excessive uptake of high cholesterol diet that increases blood lipid level. Elevated cholesterol levels contribute to changes in the arterial endothelial permeability since hyperlipidemia promotes atherosclerosis so it is associated with an increased risk of stroke incidence.^[21]

Heart Disease

Various cardiac diseases such as heart failure, mitral valvular disease, acute myocardial infarction, and atrial fibrillation increase the risk of stroke, among all of these AF is an independent risk factor for ischemic stroke.^[22] AF occurs when the upper chambers of the heart (atria) do not beat in synchronization with the lower chambers (ventricles) resulting in inadequate blood flow. Atrial fibrillation is an independent risk factor for embolic and non-embolic stroke and for all-cause mortality.^[23] The incidence and prevalence of AF increase with age.^[24] Cardioembolic ischemic stroke and cryptogenic strokes, which account for almost a third of all ischemic brain events, may be linked to AF.^[25] AF is an independent risk factor for ischemic stroke, which is 5 times higher in people who have it.^[26] A study shows that around a third of patients with ischemic stroke have clinical or subclinical AF.^[27]

Diabetes

Diabetes mellitus is a modifiable risk factor for stroke. The relative frequency of stroke symptoms was examined between cohorts with and without diabetes to assess the relative potency of diabetes mellitus as a risk factor for stroke. Atherothrombotic cerebral infarctions, transient ischemic events, reversible ischemic neurologic impairments, and multi-infarct dementia were all classed as stroke symptoms.^[28] Diabetes has been linked to an increased risk of cerebrovascular disease. The mortality from cerebrovascular disease in the diabetic population is greater by a factor of from two to five among non-diabetic persons.^[29] Diabetic patients are more likely than non-diabetic people to have atherothromboembolic cerebral infarction.^[30] Diabetes patients are more susceptible to atherosclerosis and have a higher prevalence of atherogenic risk factors, such as hypertension, obesity, and abnormal blood lipids that contribute to stroke risk.^[31] Case-control studies of stroke patients and prospective epidemiological studies have indicated that diabetes mellitus has an independent effect, with a relative risk of ischemic stroke ranging from 1.8 to 3.09 in people with diabetes.^[17]

Obesity

According to a growing body of research, obesity is linked to an increased risk of ischemic stroke in adults.^[32] In fact, the risk of ischemic stroke rises virtually linearly from a BMI of 20 to >30 kg/m², with adults with a BMI of >30 kg/m² having a 70% higher risk of ischemic stroke than those with a BMI of 25 kg/m².^[33] According to a Japanese study, obesity is linked to a higher risk of stroke as increased weight is often associated with increase in severity of hypertension. Moreover, hypertension is closely related to risk of stroke.^[34] According to a comprehensive meta analysis involving 1.8 million individuals from 97 cohort studies it was found that BMI was a strong risk factor for ischemic stroke in womens. The association of stroke was also highly mediated by hypertension, diabetes, and elevated cholesterol level. Because of weight, BP alone accounted for 65% of the risk.^[35]

Smoking

Cigarette smoking approximately doubles the risk of ischemic stroke, with a clear dosage response relationship. Smoking cessation resulted in a rapid reduction in stroke risk.^[17]

Numerous epidemiological studies showed a strong link between smoking and cerebral ischemia and subarachnoid hemorrhage stroke.^[36] Smoking causes these consequences through vessel wall alterations (atherogenesis) and hematological effects, and the relative importance of each of these pathways varies depending on the patient's age. In younger patients, smoking may be a more potent risk factor.^[37]

Alcohol Consumption

Heavy alcohol use raises the relative risk of any stroke, whereas light to moderate alcohol consumption may protect against ischemic stroke. Frequent alcohol use was linked to an increased risk of small artery blockage in ischemic stroke.^[38] Alcohol consumption appears to have a more direct linear link with hemorrhagic stroke, with even little doses of alcohol appearing to enhance bleeding risk. Heavy alcohol consumption has been associated to hypertension and poor BP control in hypertensive patients who drink.^[39]

Oral Contraceptives

Oral contraceptives with an oestrogen content >50 g were substantially linked to an increased risk of stroke. In more than 3.6 million woman years of observation, a trial of low-dose oral contraceptives (50 g oestrogen) found no increased risk of stroke.^[40]

Physical Inactivity

Physical inactivity has been linked to a variety of negative health outcomes, including stroke. Physically active people have a lower risk of stroke and stroke mortality than inactive people.^[41]

Physical activity and stroke are related because physical activity associated with decrease in BP, reduction in diabetes mellitus, and reduction in excess body weight that may help in reducing the risk of stroke.^[42] Physical inactivity is a preventable cause of stroke in those over the age of 80. Improved physical activity may lower the risk of stroke in this group of people.^[43]

Diet

Diet and nutrition have an impact on the risk of stroke and other stroke risk factors such diabetes, hypertension, and dyslipidemia.^[44] Nutritional consumption has been demonstrated to affect stroke risk variables in observational studies.^[45]

Salt

Several studies have found a link between BP and dietary sodium chloride, as well as an inverse relationship between dietary potassium, calcium, and magnesium.^[46] Greater potassium consumption has been linked to a lower stroke death rate, while low potassium intake has been linked to a higher stroke rate.

Vegetables and fruits

According to epidemiological research, consumption of green-yellow vegetables, fruits, fiber, or whole grain, but not refined grain, appears to be protective against ischemic stroke.^[47]

Dietary fat

Dietary fat has an effect on blood cholesterol levels, it is likely to contribute to a high cholesterol level and, as a result, an increased risk of stroke.^[48]

Protein

In women with a history of hypertension, a low diet of saturated fat and animal protein has been linked to an increased risk of cerebral hemorrhage.^[49]

MODIFIABLE RISK FACTORS

Age

The risk of stroke increases with age, with the risk doubling every decade after the age of 55.^[50] Strokes in young adults are reported as being uncommon accounting for 10%–15% of all stroke cases.^[51] Since 2009, a few studies on the incidence of stroke in young adults have been published. A Finnish study looked at 1008 patients who had an ischemic stroke and were between the ages of 15 and 49.^[52] Studies on risk factors showed that age has been identified as markers of risk for stroke, cannot be modified.

Gender

The incidence of stroke is higher in males than in women across all age groups, and women are on average several years older than men when they have their first stroke. Stroke is more common in men until they reach the age of 80, at which point it becomes more common in women.^[53] Men have a 1.25 times higher stroke rate than women, but because women live longer than men, more women than men die of stroke each year.^[54] The increased risk of stroke in young women is most likely due to risks associated with pregnancy and the postpartum period, as well as other hormonal factors including the use of hormone medication and oral contraceptives. Women suffer from strokes at a higher rate than men, due to their longer life expectancy.^[55]

Genetic

Stroke risk is influenced by hereditary factors.

- Specific rare single gene disorders (e.g., cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) may contribute to individual familial syndromes in which stroke is the primary or only manifestation (e.g., cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy).
- Single gene defects can lead to a multisystem condition, with stroke being one of the symptoms (e.g., sickle cell anemia).
- The individual impact of such polymorphisms is viewed as minor, several common variants of genetic polymorphisms have been linked to stroke risk (e.g., variants in 9p21).

- Genetic causes of conventional stroke risk factors, such as AF, diabetes mellitus, and hypertension, are also, not surprisingly, associated with the risk of stroke.^[56,57]

Race

Stroke racial discrepancies have been well-documented. When compared to Whites, Blacks have twice the risk of having an incident stroke and have a higher stroke-related mortality rate.^[58] The “Strong Heart Study”^[5] was used to estimate the incidence of stroke and explicate stroke risk factors among American-Indians, and the results revealed that American-Indians have a higher stroke rate.^[59]

OTHER PSYCHOLOGICAL RISK FACTORS

Depression

A population-based cohort study conducted in the NHANES on 6095 stroke-free White and Black men and women aged 25–74 years found a prospective link between depression and stroke. The people with depression are more prone to have a risk of stroke.^[60]

Stress

Both acute and persistent emotional stresses have been linked to an increased risk of stroke. Several possible methods for the cause are suggested. By modifying sympathomimetic activity, influencing BP reactivity, cerebral endothelium, coagulation, or heart rhythm, stress can raise the risk of cerebrovascular illness.^[61] Stress, on the other hand, is not recognized as a known risk factor for stroke in the current international guidelines.

CONCLUSION

Burden of stroke is increasing globally. The foremost strategy to reducing morbidity and mortality related to stroke is to control associated risk factors. There are several modifiable risk factors such as hypertension, diabetes mellitus, hyperlipidemia, obesity, smoking, nutrition, and physical inactivity that can be managed by lifestyle changes. Moreover, some are non-modifiable such as age, gender genetic, and race. There is a need further researches on stroke associated psychological factors such as stress and depression. In addition, need is to developing the interventions that can help reducing the impact of disease. Hopefully better understanding of stroke associated risk factors in the general population may lead to improved prevention of stroke.

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