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STROKE: EPIDEMIOLOGY, PATHOPHYSIOLOGY, DIAGNOSIS, MANAGEMENT, AND FUTURE DIRECTIONS - A COMPREHENSIVE REVIEW

Aravinth M.[1]*, Praveenkumar M.[2], Vignesh S.[1], Anandhasivam T.[1] and Vinothini A.[1]

[1*]Student, SS Institute of Pharmacy, Sankari, Salem-637301.

[2]Assistant Professor, SS Institute of Pharmacy, Sankari, Salem-637301.

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***Corresponding Author**

Aravinth M.

Student, SS Institute of Pharmacy, Sankari, Salem-637301.

ABSTRACT

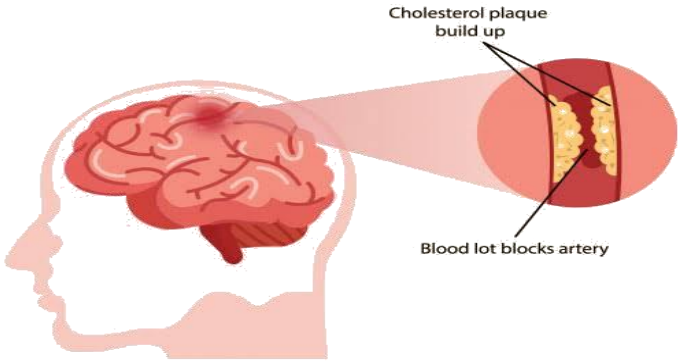
Stroke, or cerebrovascular accident (CVA), is a leading cause of death and disability worldwide, resulting from the sudden disruption of cerebral blood flow. It can be classified into ischemic strokes, caused by arterial blockage, and hemorrhagic strokes, resulting from vessel rupture and bleeding. This article explores the underlying pathological mechanisms, including excitotoxicity, oxidative stress, and blood-brain barrier disruption, and highlights the histopathological differences between ischemic and hemorrhagic types. The global burden of stroke is rising, particularly in low- and middle-income countries, with significant age, gender, and geographic disparities. Major risk factors include both modifiable (e.g., hypertension, diabetes, smoking, obesity) and non-modifiable (e.g., age, sex, genetic predisposition) elements. Timely diagnosis and intervention—such as thrombolysis, mechanical thrombectomy, or surgical management—are critical in improving outcomes. Rehabilitation and preventive strategies focused on risk factor management are essential for reducing recurrence and improving quality of life. Continued research and public health initiatives are vital to mitigate the global impact of stroke.

KEYWORDS: *Stroke, Blood-Brain Barrier, Hemorrhagic Stroke, Ischemic Stroke, Thrombolysis.*

INTRODUCTION

Stroke, also known as a cerebrovascular accident (CVA), is one of the main causes of illness and death around the world. It causes serious health problems and has a major impact on

individuals, families, and society. A stroke happens when there is a sudden problem in the brain's blood supply. This can cause the brain to malfunction. According to the World Health Organization (WHO), a stroke is defined as a sudden issue in brain function that lasts more than 24 hours and is caused by problems in the blood vessels of the brain. There are different types of strokes. These include ischemic strokes, where blood flow to part of the brain is blocked, often by a blood clot. Other types include hemorrhagic strokes, where bleeding occurs inside the brain (intracerebral hemorrhage) or around the brain (subarachnoid hemorrhage). Another less common type is cerebral venous sinus thrombosis, where a blood clot forms in the brain's veins. Stroke is the third most common cause of death in developed countries, after heart disease and cancer. Each year, about 700,000 people are affected by strokes. While many people survive a stroke, it often leaves them with long-term health issues. It is estimated that around 30% of stroke survivors have serious and lasting disabilities. These can include problems with movement, speech, memory, or the ability to care for themselves. Around 20% of stroke survivors may also have other lasting effects, though they may be less severe. Because of the high number of people affected and the serious health problems it causes, stroke is a major public health concern. Understanding the types of stroke and how to manage them is very important for reducing their impact.[1]



Pathological Mechanisms and Histopathological Features of Stroke

Stroke is a complex neurological condition that occurs when blood flow to the brain suddenly stops, resulting in serious tissue damage. The mechanisms behind stroke differ based on whether it is ischemic or hemorrhagic, but both types lead to neuron injury and loss of brain function. In ischemic stroke, an obstruction like a clot blocks blood flow. This causes a critical shortage of oxygen and nutrients in the affected brain areas. The lack of blood flow triggers a series of cellular events that result in neuron injury and death. One major process

involved is excitotoxicity, where too much glutamate overstimulates neurons, leading to toxic calcium influx and damage. Additionally, ischemia causes oxidative stress through the production of reactive oxygen species, further harming cell membranes, proteins, and DNA. Inflammation plays a significant role, too. Activated microglia and immune cells release inflammatory substances that worsen neuron injury. Another key mechanism is the disruption of the blood-brain barrier (BBB), which normally protects the brain from harmful substances. In a stroke, the BBB becomes more permeable, allowing fluids and proteins to leak into brain tissue and causing vasogenic edema. This swelling increases pressure inside the skull and leads to more neuron damage and dysfunction.[2]

Hemorrhagic stroke occurs when a blood vessel in the brain ruptures, spilling blood into brain tissue or surrounding areas. The pooling of blood forms a hematoma that compresses and destroys brain tissue. Additionally, components of the blood, like hemoglobin and iron, have toxic effects that increase oxidative stress and inflammation in the affected area.[3]

Global Stroke Overview

Stroke is the 2nd leading cause of death worldwide Affects ~13.7 million people; ~5.5 million die annually87% are ischemic strokes, increasing due to better survival and clinical care Primary hemorrhages are most common; secondary hemorrhages make up 10-25% Stroke incidence doubled in low/middle-income countries (1990-2016), but decreased 42% in high-income countries. Despite some prevalence decline, the socio-economic burden increased due to demographic shifts.[4,5,6]

Age-Specific Trends

- Stroke risk doubles after age 55
- Strokes in younger adults (20-54) increased from 12.9% to 18.6% globally (1990-2016). Death rates standardized by age dropped by 36.2%.
- Highest incidence in China (331–378 per 100,000 life years), then Eastern Europe, and lowest in Latin America.[7]

Gender Differences

- Women have higher stroke incidence at younger ages (due to pregnancy, contraceptives, migraines).
- Men see an increased stroke with age.
- Women have higher severity and fatality rates.

- Men's strokes are more linked to smoking, alcohol, and heart disease.
- Geographic & Racial Variation
- Stroke rates vary globally, influenced by air pollution, hypertension, lifestyle (diet, physical activity, smoking).
- Environmental pollutants (lead, cadmium) contribute to variation.
- In the US, racial disparities are observed between Black and White populations.

Risk factors for stroke

Stroke risk factors fall into two main categories: modifiable and non-modifiable. Modifiable risk factors can change with lifestyle adjustments or medical treatments. These include high blood pressure, high cholesterol, smoking, diabetes, obesity, lack of physical activity, and consuming too much alcohol. Non-modifiable risk factors cannot be changed and include age, sex, family history, and race or ethnicity. Certain medical issues, like heart disease, a previous stroke, or TIA, and blood disorders, can also raise the risk of stroke.

Modifiable Risk Factor

High Blood Pressure: Also known as hypertension, high blood pressure harms blood vessels and raises the chance of having a stroke. It is a major risk factor for both ischemic and hemorrhagic strokes.

High Cholesterol: High cholesterol levels can cause plaque to build up in arteries, which leads to blood clots and increases stroke risk.

Smoking: Smoking harms blood vessels, raises blood pressure, and boosts the risk of blood clots, contributing to strokes.

Diabetes: Diabetes can damage blood vessels and elevate the risk of stroke.

Obesity: Being overweight or obese is connected to several stroke risk factors, like high blood pressure, high cholesterol, and diabetes.

Physical Inactivity: Not getting enough exercise relates to obesity, high blood pressure, high cholesterol, and diabetes, all of which heighten stroke risk.

Excessive Alcohol Consumption: Drinking too much can raise blood pressure and triglyceride levels, which increases stroke risk.

Diet: A diet high in saturated fats, trans fats, and cholesterol but low in fruits and vegetables can raise the risk of stroke. Sleep Apnea: Obstructive sleep apnea, where breathing repeatedly stops and starts during sleep, is linked to a higher risk of stroke.

COVID-19 Infection: Infection with COVID-19 has been associated with an increased risk of stroke, especially in people with other risk factors.[8]

Non-Modifiable Risk Factors

Age: The risk of stroke goes up with age, with most strokes happening in people over 65.

Sex: Men generally have a higher risk of stroke than women, although this difference may lessen with age.

Family History: A family history of stroke or other heart diseases can increase a person's risk.

Race and Ethnicity

Certain ethnic groups, including Black, Alaska Native, American Indian, and Hispanic populations, have a higher risk of stroke.

Genetic Factors

Some genetic disorders can make individuals more prone to strokes.[9]

Prior Stroke or TIA: Having had a previous stroke or transient ischemic attack (TIA) greatly raises the risk of future strokes.[10]

Heart Conditions: Conditions like atrial fibrillation, heart valve disease, and heart failure increase the risk of stroke.

Blood Vessel Problems: Abnormalities in blood vessels, such as aneurysms or arteriovenous malformations (AVMs), can heighten stroke risk.

Blood Disorders: Certain blood disorders, like sickle cell anemia, can increase stroke risk.

Autoimmune Conditions: Some autoimmune conditions, such as lupus, can also raise the risk of stroke.

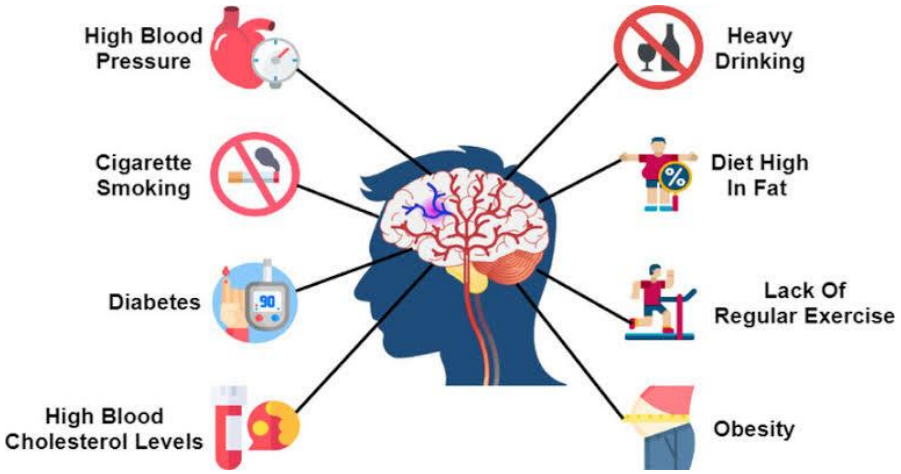
Infections: Certain infections, like bacterial endocarditis, can increase stroke risk.[11,12,13,14]

Other Factors

- Pregnancy: Pregnancy and the postpartum period can increase stroke risk, especially in women with preeclampsia.

Oral Contraceptives

- Using birth control pills, particularly with other risk factors, can increase stroke risk.



Hormone Replacement Therapy

- Hormone replacement therapy can also raise stroke risk in some individuals.
- Understanding these risk factors is vital for preventing and detecting strokes early. While some cannot be changed, many can be adjusted through lifestyle choices and medical treatments, which can significantly lower the overall risk.[15]

Classification

1. Ischemic Stroke

Cause: Blockage of an artery, usually by a blood clot or plaque buildup, preventing blood flow to **the brain.**

Prevalence: Approximately 87% of all strokes are ischemic.

Subtypes:

Thrombotic: A Blood clot forms within a brain artery.

Embolic: A Blood clot or plaque travels from elsewhere in the body and lodges in a brain artery.

Small vessel occlusion (lacunar): Affects small arteries deep in the brain.

Cardioembolic: A Blood clot originates in the heart and travels to the brain.

Cryptogenic: The Cause is unknown despite investigation.

2. Hemorrhagic Stroke

Cause: Rupture of a blood vessel in the brain, causing bleeding into brain tissue or surrounding spaces.

Prevalence: Approximately 13% of all strokes are hemorrhagic.

Subtypes:

Intracerebral hemorrhage (ICH): Bleeding within the brain tissue.

Subarachnoid hemorrhage (SAH): Bleeding into the space between the brain and the skull.

3. Transient Ischemic Attack (TIA)

Cause

- Temporary disruption of blood flow to the brain, often due to a blood clot that dislodges on its own.

Symptoms

- Similar to ischemic stroke but resolves within minutes to hours, with no lasting damage.[16]

Diagnosis test and figure

Figure: 1.

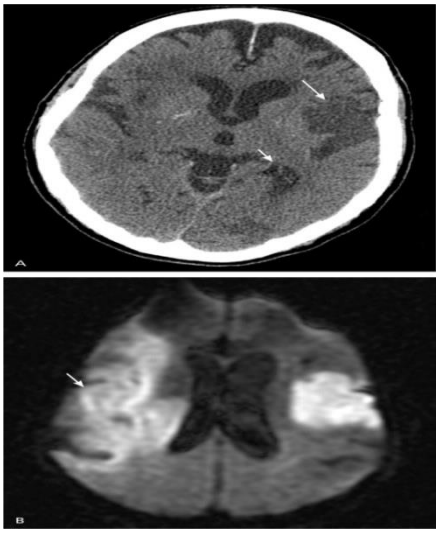
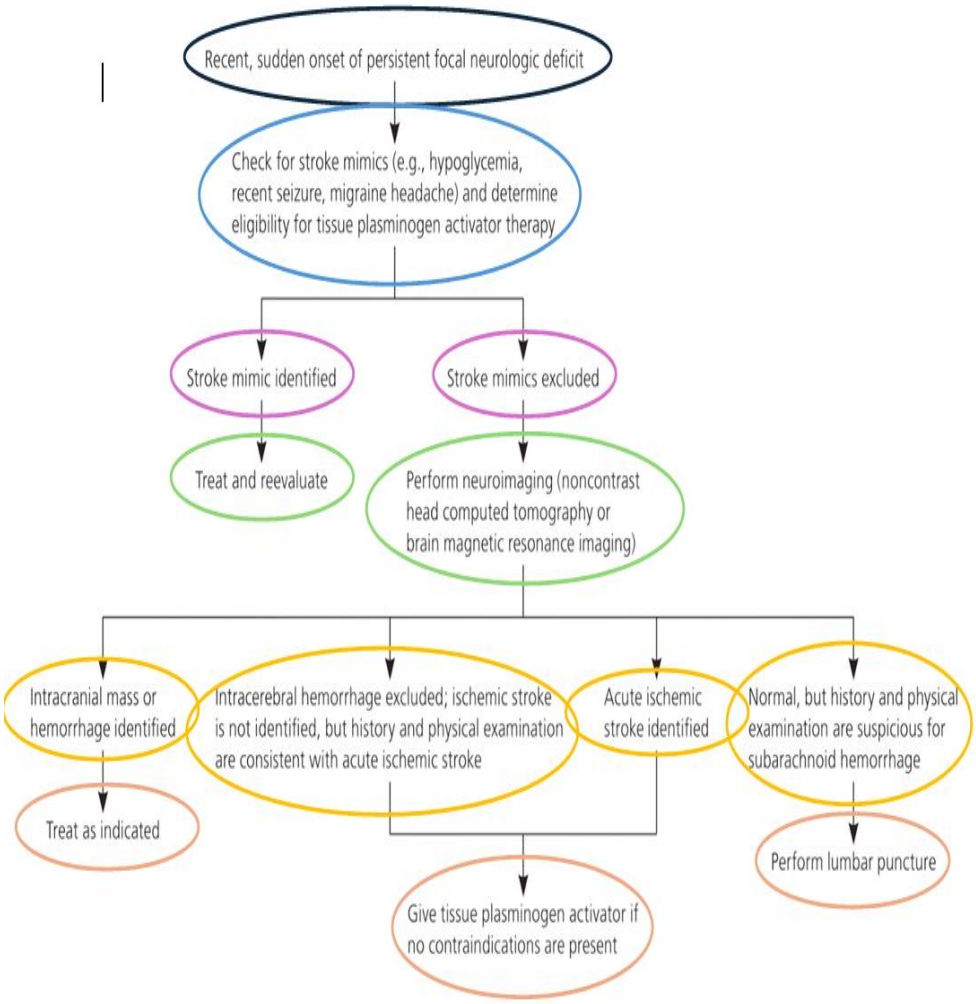


Figure: 2.


Recent, sudden onset of persistent focal neurologic deficit
Check for stroke mimics (e.g., hypoglycemia, recent seizure, migraine headache) and determine eligibility for tissue plasminogen activator therapy
Stroke mimic identified
Stroke mimics excluded
Treat and reevaluate
Perform neuroimaging (noncontrast head computed tomography or brain magnetic resonance imaging)
Intracranial mass or hemorrhage identified
Intracerebral hemorrhage excluded; ischemic stroke is not identified, but history and physical examination are consistent with acute ischemic stroke
Acute ischemic stroke identified
Normal, but history and physical examination are suspicious for subarachnoid hemorrhage
Treat as indicated
Perform lumbar puncture
Give tissue plasminogen activator if no contraindications are present

Treatment

1. Ischemic Stroke (≈87% of all strokes)

Cause: A Blood clot blocks a blood vessel in the brain.

Goal: Restore blood flow to the brain as quickly as possible.

Emergency Treatment

- Intravenous thrombolysis (tPA)
- Tissue plasminogen activator (alteplase) can dissolve the clot.
- Must be given within 4.5 hours of symptom onset (the sooner, the better).

Mechanical thrombectomy

- Removal of the clot using a catheter through a large artery (usually within 6–24 hours of symptom onset).
- Used in certain large vessel occlusions.

Other treatments

Antiplatelet drugs (e.g., aspirin)

- Often started within 24–48 hours after onset (not given if tPA is used immediately).

Anticoagulants

- For strokes caused by atrial fibrillation or other embolic sources (e.g., warfarin, DOACs).

Statins

- To reduce cholesterol and the risk of future strokes.

Blood pressure control

- Managed carefully post-stroke.

2. Hemorrhagic Stroke (bleeding in the brain)

Cause

- Ruptured blood vessel (e.g., due to high blood pressure or aneurysm).

Goal

- Stop the bleeding and reduce pressure on the brain.

Emergency Treatment

Blood pressure control

- Intensive lowering of BP is high.

Surgery

- Craniotomy to remove the blood and relieve pressure.
- Aneurysm clipping or coil embolization if an aneurysm caused the bleed.

Medications

- To reverse anticoagulants if the patient was on blood thinners.

3. Post-Stroke Care & Rehabilitation

Physical therapy: Regain mobility and strength.

Occupational therapy: Relearn daily tasks.

Speech therapy: For language and swallowing issues.

Psychological support: Address depression, anxiety, and cognitive deficits.

1. Control High Blood Pressure (Hypertension)

- The most important modifiable risk factor.
- Target: usually <130/80 mmHg (varies by guidelines and patient risk).
- Lifestyle and/or medications (e.g., ACE inhibitors, diuretics).

2. Manage Diabetes

- Keep blood glucose in the target range.
- Use medications like metformin, GLP-1 agonists, or insulin if needed.
- Monitor HbA1c (goal typically <7% for most people).

3. Control Cholesterol

- Use of statins (e.g., atorvastatin) to reduce LDL cholesterol.
- Especially important for people with atherosclerosis or prior cardiovascular events.

4. Treat Atrial Fibrillation (AFib)

- Irregular heart rhythm increases the risk of embolic stroke.
- Oral anticoagulants (e.g., warfarin, apixaban, rivaroxaban) reduce stroke risk significantly.

5. Healthy Lifestyle Habits

- Diet: Mediterranean or DASH diet (rich in fruits, vegetables, whole grains, healthy fats).
- Exercise: At least 150 minutes/week of moderate activity.
- Weight control: Maintain a healthy BMI.
- No smoking: Eliminating tobacco use lowers stroke risk.
- Limit alcohol: If consumed, do so in moderation (≤1 drink/day for women, ≤2 for men).

6. Antiplatelet Therapy (for high-risk individuals)

- Aspirin or clopidogrel may be prescribed for people with:
- History of TIA or stroke.
- Known atherosclerosis.
- Not recommended for low-risk individuals due to bleeding risks.

7. Regular Medical Checkups

- Monitor and treat:
- High blood pressure
- Diabetes
- High cholesterol
- Heart rhythm disorders.[17]

CONCLUSION

Stroke remains a significant global health issue, contributing to substantial morbidity, mortality, and long-term disability. This review highlights the complex pathophysiology of both ischemic and hemorrhagic strokes, the wide range of modifiable and non-modifiable risk factors, and the global trends influenced by age, gender, geography, and socio-economic status. Advances in acute treatment—such as thrombolysis and mechanical thrombectomy—as well as comprehensive rehabilitation strategies, have improved outcomes. However, the growing burden in low- and middle-income countries and among younger populations underscores the urgent need for strengthened prevention, early detection, and equitable access to care. Ongoing research, combined with public health initiatives, is essential to reduce stroke incidence, improve recovery, and minimize the global impact of this debilitating condition.

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