

REVIEW ARTICLE



# Comprehensive Review on Burden of Strokes and Cardiovascular Diseases in the Indian Scenario

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**Abstract:** Heart disease and stroke are both types of cardiovascular diseases (CVD) and are among the most widespread and costly health problems as per statistics. 31% of all global deaths are due to CVD. Classical symptoms include angina, discomfort in arms & shoulders, shortness of breath, dizziness, cold, sweats, nausea and fatigue. The major risk factors for CVD include smoking, physical inactivity, excess body weight and unhealthy dietary pattern. Other factors that can contribute to CVD are blood pressure, cholesterol, impaired glucose control and sleep. There are a range of major clinical heart and CVD conditions that include stroke, congenital heart disease, coronary heart disease, rhythmic disorders, subclinical atherosclerosis, vascular disease, peripheral artery disease, heart failure and venous disease. This paper reviews different types of CVD conditions, core health behaviours and the associated outcomes such as quality of care, medical procedures and economic burden. This review is an attempt to improve the understanding of heart diseases and stroke that will be helpful on preventing and treating heart disease and improving overall cardiovascular health.

**Keywords:** Heart, cardiovascular disease, atherosclerosis, heart failure, health, hypertension, stroke.

## 1. INTRODUCTION

Heart diseases or cardiovascular diseases (CVD) are heart conditions that include diseased vessels, structural problems and blood clots. Over the past decade, ischemic heart diseases and strokes have remained the top two causes of death. An estimated 17.9 million people died from CVDs in 2019, representing 32% of all global deaths. Of these deaths, 85% were due to heart attack and stroke. CVD includes coronary artery diseases (CAD), stroke, heart failure, hypertensive heart disease, congenital heart disease, *etc.* Typical symptoms of an underlying cardiovascular issue involve pain or pressure in the chest which may indicate angina, pain or discomfort in the arms, left shoulder, elbows, jaw or back, shortness of breath, dizziness, cold, sweats, nausea and fatigue [1,2].

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Cardiovascular diseases (CVD) are the leading cause of death worldwide except Africa. This condition is found to be more common and increasing in developing countries. Eastern Europe accounts the highest estimated rate of ischemic heart disease (IHD) in 2015. IHD is estimated for almost one-half of all CVD cases in Central Asia and Eastern Europe, but a smaller proportion in Central Europe. Other cardiovascular and circulatory diseases made up a larger proportion of total cases in Eastern sub-Saharan Africa, the Middle East / North Africa region, and South Asia. More than one-quarter of cases in sub-Saharan Africa were due to other cardiovascular and circulatory diseases. The lowest estimated rate of IHD was in Central sub-Saharan Africa. The death rate IHD was highest in Central Asia (336 per 100,000) and Eastern Europe (326 per 100,000), followed by Oceania, South Asia, and the Middle East / North Africa. High-income regions of North America and Latin America had high rates of total CVD deaths that were due to IHD [3]. Hypertensive heart disease was the fourth-highest ranked CVD in 2015; however, it ranked lower in high-income regions such as Australia, high-income Asia Pacific, and Western Europe. Oceania was the region with the highest rate of stroke (1,003 per 100,000), followed by Eastern Europe, Central Asia, and Southeast Asia. The lowest stroke rate was in Central Latin America (177 per 100,000). CVD deaths due to cardiomyopathy and myocarditis were most common in the regions of Southern sub-Saharan Africa and tropical Latin America [4].

## 2. HEALTH BEHAVIOURS

### 2.1. Smoking/Tobacco Use

Tobacco smoking is a major risk factor for CVD and stroke. Electronic cigarette use, which involves inhalation of a vaporized liquid that contains nicotine, solvents, and flavouring (“vaping”) also contributes to CVD and stroke. The frequency of cigarette smokers was found highest in the Midwest (18.5%) and lowest in the West (12.3%). 17.5% of males and 13.5% of females are current smokers. When cigarette smoke is taken in, the blood that is distributed to the rest of the body becomes contaminated with the smoke’s chemicals. These chemicals can damage heart and blood vessels that can lead to cardiovascular disease (CVD), the leading cause of all deaths in the United States. Cigarette smoke can also cause CVD by changing blood chemistry and causing plaque waxy substance comprised of cholesterol, scar tissue, calcium, fat, and other material to build up in the arteries, the major blood vessels that carry blood from your heart to your body. This plaque build-up can lead to a disease called atherosclerosis. Current smokers have a 2 to 4 - times increased risk of stroke compared with non-smokers or those who have quit for >10 years. Smokers who quit smoking at 25 to 34 years of age gained 10 years of life. Those aged 35 to 44 years gained 9 years and those aged 45 to 54 years gained 6 years of life, compared to those who continued smoking [5,6].

### 2.2. Physical Inactivity

Physical inactivity or being sedentary is when an individual doesn’t move body for long periods of time. This can include sitting or lying on the couch watching TV, and sitting at a desk or computer. This is one of a major risk factor for heart diseases and stroke. In 2015, 41.7% of high school students used a computer for activities other than school work (*e.g.*, videogames) for  $\geq 3$  hours per day on an average school day. Being active, one can reduce the risk of developing some heart and circulatory diseases by as much as 35%. Regular physical activity helps control blood pressure and keep it within healthy levels, raises levels of good cholesterol, and reduces the bad cholesterols. Only about 22 % of Americans report regular sustained physical activity (activity of any intensity lasting 30 minutes or more 5 times a week). Fifteen percent of Americans report vigorous activity (activity intense enough to make the heart beat fast). Risk of heart disease decreased when people took up leisure-time exercise, with people exercising for 36 minutes of brisk walking per day having less than half the risk of non-exerciser [6,7].

### 2.3. Nutrition

The European Society of Cardiology (ESC) and American Heart Association Nutrition Committee strongly recommend the daily consumption of both fruits and vegetables in order to reduce CVD risk. An

olive oil rich diet also reduces the risk of heart diseases and stroke. Nuts, mainly peanuts and walnuts have demonstrated to reduce the risk of CVD. It has been observed that the deficiency of some of the nutrients can result in atherosclerotic disease. A wide number of studies have reported that dietary fibres intake decreases cholesterol concentrations and BP, while a deficiency of fibres intake can lead to CVD development. Micro nutrients also protect against CVD by reducing the endothelial cell damage, improving the production of NO and inhibiting the oxidation of LDL-c. Omega-3 Fatty Acids is a potential anti-atherogenic agent in atherosclerotic process. Thus, healthy dietary habits and active lifestyle should be promoted among children and adults to combat diseases related to heart [8].

## 2.4. Overweight and Obesity

Overweight and obesity are defined by the World Health Organization as abnormal or excessive fat that accumulates and present a risk to health. A person with a BMI of 30 or more is generally considered obese. A person with a BMI equal to or more than 25 is considered overweight. CVD mortality and morbidity has been shown to be elevated in individuals who are overweight, particularly with central deposition of adipose tissues. Overweight and obesity contributes directly to cardiovascular risk factor. Abdominal obesity determined by waist circumference is used as a cardiovascular disease marker. Patients with obesity experience CVD at early stages of life have a shorter average lifespan compared to people with normal weight. Patients who have undergone bariatric surgery had reduced risk of CAD when compared to non-surgical patients with obesity. An estimate of 2.6 million deaths worldwide and 2.3% of the global burden of disease are caused by obesity [9].

Obesity also increases the risk of High Blood Pressure (HBP). Persistent hypertension is one of the risk factors for stroke, myocardial infarction (MI), heart failure, and arterial aneurysm, and is a leading cause of chronic kidney failure. Moderate elevation of arterial blood pressure leads to shortened life expectancy, which also increases the risk of heart diseases. According to 2015 to 2016 data from NHANES (NCHS/CDC), the overall rate of obesity was 18.5%. By age group, the rate of obesity for children aged 2 to 5 years was 13.9%, for children aged 6 to 11 years, the rate was 18.4%, and for adolescents aged 12 to 19 years, the rate was 20.6% [8,9,10].

## 3. HEALTH FACTORS AND OTHER RISK FACTORS

### 3.1. High Blood Cholesterol and Other Lipids

Cholesterol is the primary risk factor for development of atherosclerosis. Abnormal blood lipid (fat) levels have a strong connection with the risk of coronary artery disease, heart attack and coronary death. Total cholesterol, HDL and LDL for different populations is given in Table 1. When there is too much cholesterol in blood, it builds up in the walls of arteries, causing a process called atherosclerosis, a form of heart disease. The arteries become narrowed and blood flow to the heart muscle is slowed down or blocked. The blood carries oxygen to the heart, and if not enough blood and oxygen reaches heart, the person can suffer from anginal pain. If the blood supply to a portion of the heart is completely cut off by a major blockage, the result is a heart attack [9,10,11].

**Table 1. Total cholesterol, HDL and LDL for different populations.**

Parameter	Ideal/Desirable Range	North American Adults	European Adults	Asian Populations
<b>Total Cholesterol</b>	< 200 mg/dL	180-220 mg/dL	< 200 mg/dL	Typically slightly lower
<b>HDL Cholesterol</b>	≥ 60 mg/dL (protective)	40-60 mg/dL	≥ 60 mg/dL	Slightly lower average
<b>LDL Cholesterol</b>	< 100 mg/dL (optimal)	< 100 mg/dL	≥ 60 mg/dL	Typically slightly lower

### 3.2. High Blood Pressure

High Blood Pressure (HBP) is a major risk factor for CVD and stroke. 54% of strokes and 47% of coronary heart diseases, worldwide, are due to high BP. The frequency of hypertension increases with age

(Table 2). HBP usually develops over time. It can happen because of unhealthy lifestyle choices, for instance, not getting enough regular physical activity. Certain health conditions, such as diabetes and having obesity can also increase the risk for developing high blood pressure. High blood pressure can also damage arteries by making them less elastic thereby decreasing the flow of blood and oxygen to heart leading to heart disease [10,12,13].

**Table 2. Frequency of hypertension increases with age.**

Age Group	Hypertension Prevalence	Precipitating Factors
Young Adults (18-39 years)	Less common, but increasing	Rising obesity, lifestyle factors, and genetic predisposition
Middle age adults (40-59 years)	Approximately 50-60%	Obesity, sedentary lifestyle, and accumulation of risk factors
Older Adults (60+)	Over 70%	Arterial stiffening, changes in blood vessel structure, and cumulative risk factors

### 3.3. Diabetes Mellitus

Heart failure is highly frequent amongst patients with diabetes mellitus. Diabetic patients have an increased risk of developing heart failure because of the abnormal cardiac handling of glucose and free fatty acids (FFAs). The metabolic risk of diabetes in heart failure is heightened by the effect of most anti-diabetic medications as the use of certain anti-diabetic agents increase the risk of mortality and hospitalization for heart failure both in patients, with and without heart failure. In diabetic patients, heart failure develops not only because of the underlying coronary artery disease, but also because of the multiple pathophysiological and metabolic abnormalities induced by altered glucose metabolism. Beta-blockers and angiotensin-converting enzyme inhibitors are beneficial in patients with diabetes mellitus and their use is associated with reduced mortality and hospitalizations. Glucose-lowering agents are known to increase the risk of cardiovascular events especially when a tight glycaemic control is pursued. Over time, high blood glucose from diabetes can damage your blood vessels and the nerves that control your heart and blood vessels. The longer you have diabetes, higher the chances to develop heart disease. [14,15].

### 3.4. Metabolic Syndrome

Metabolic syndrome is a cluster of conditions that occur together, increasing risk of heart disease, stroke and type 2 - diabetes. These conditions include elevated blood pressure, high blood sugar, excess body fat around the waist, and abnormal cholesterol or triglyceride levels. The risk of heart disease in people with metabolic syndrome is almost as high as those with diabetes. CVD is the primary clinical outcome of metabolic syndrome. In the absence of diabetes, the metabolic syndrome generally did not raise 10 - year risk for CHD to >20%. Insulin resistance may also increase the risk for metabolic syndrome. It is a condition in which the body can't use its insulin properly. A fatty liver, polycystic ovary syndrome, gallstones and breathing problems during sleep are some of the conditions that increase the risk of metabolic syndrome. Metabolic syndrome is diagnosed when someone has three or more of these risk factors: high blood glucose (sugar), low levels of HDL ("good") cholesterol in the blood, high levels of triglycerides in the blood, large waist circumference or "apple-shaped" body, and high blood pressure [16].

### 3.5. Kidney Diseases

Patients with chronic kidney diseases (CKD) have a strong risk of CVD. Heart disease is the most common cause of death among people on dialysis. When an individual has heart disease, the heart may not pump blood in the right way and may become too full of blood. This causes pressure to build in the main vein connected to kidneys which may lead to a blockage and a reduced supply of oxygen rich blood to the kidneys resulting in kidney disease. Nearly two-thirds (64.5%) of CKD patients are 66 years of age or older and have CVD when compared with approximately one-third (32.4%) of patients without CKD in this age group. CVD is a leading cause of death for people with CKD. Statistics indicate that 1 in 10 persons in the general population are estimated to have some form of chronic kidney disorder (CKD). About

175,000 new people have kidney failure (stage V CKD) every year in India and require dialysis and / or kidney transplantation [17, 18].

### **3.6. Sleep**

Sleep can be characterized in many different ways including quantity of sleep (sleep duration), quality of sleep, or the presence of a sleep disorder, such as insomnia. Infants 4 to 12 months old should sleep 12 to 16 hours per day; children 1 to 2 years of age should sleep 11 to 14 hours per day; children 3 to 5 years of age should sleep 10 to 13 hours per day; children 6 to 12 years of age should sleep 9 to 12 hours per day; and adolescents 13 to 18 years of age should sleep 8 to 10 hours per day. Females have a greater risk of insomnia than males. Data from the CDC indicated that the age-adjusted prevalence of healthy sleep duration was lower among Native Hawaiians / Pacific Islanders (53.7%), NH blacks (54.2%), multiracial NH people (53.6%), and American Indians / Alaska Natives (59.6%) compared with NH whites (66.8%), Hispanics (65.5%), and Asians (62.5%). A 2011 *European Heart Journal* review of 15 medical studies involving almost 475,000 people found that short sleepers had a 48% increased risk of developing or dying from coronary heart disease (CHD) in a 7 to 25-year follow-up period (depending on the study) and a 15% greater risk of developing or dying from stroke during this same time. Interestingly, long sleepers those who averaged nine or more hours a night also showed a 38% increased risk of developing or dying from CHD and a 65% increased risk of stroke. Research has found that sleep deprivation contributes to atherosclerosis. Plaque forms as a consequence of inflammation, which involves white blood cells that are produced by the immune system to collect in the arteries. Poor sleep triggers chronic inflammation, which contributes to plaque formation and hardening of the arteries. People who slept less than seven hours per night had an elevated risk of heart failure. Heart failure was also more common in people who had other indicators of unhealthy sleep including insomnia symptoms, daytime sleepiness, snoring, and being an evening person [19,20].

## **4. TYPES OF CVD**

### **4.1. Total Cardiovascular Diseases**

Cardiovascular diseases (CVDs) are a group of disorders of the heart and blood vessels and they include:

- Coronary Heart Disease – disease of the blood vessels supplying the heart muscle;
- Cerebrovascular Disease – disease of the blood vessels supplying the brain;
- Peripheral Arterial Disease – disease of blood vessels supplying the arms and legs;
- Rheumatic Heart Disease – damage to the heart muscle and heart valves from rheumatic fever, caused by streptococcal bacteria;
- Congenital Heart Disease – malformations of heart structure existing at birth;
- Deep vein thrombosis and pulmonary embolism – blood clots in the leg veins, which can dislodge and move to the heart and lungs.

The most important behavioural risk factors of heart disease and stroke are unhealthy diet, physical inactivity, tobacco use and harmful use of alcohol, age-adjusted prevalence of HD among whites, blacks, Hispanics, and Asians was 11.0%, 9.7%, 7.4%, and 6.1%, respectively [21,22].

### **4.2. Stroke (Cerebrovascular Diseases)**

Stroke is the sudden death of brain cells due to lack of oxygen, caused by blockage of blood flow or rupture of an artery to the brain. There are Three main causes of strokes:

1. Ischemic - where the blood supply is stopped because of a blood clot, accounting for 85% of all cases.
2. Haemorrhagic - where a weakened blood vessel supplying the brain bursts.

3. **Cardiogenic Stroke** - A cardiogenic stroke happens when heart problems like atrial fibrillation, heart attacks, or the use of artificial heart valves cause a blood clot to travel from the heart to the brain. [23,24,25].

The major risk factor for stroke includes high blood pressure, diabetes, high LDL cholesterol levels, family history and genetics, heart and blood vessel diseases. Stroke is one of the leading causes of death and disability in India. The estimated adjusted prevalence rate of stroke range approximately 84-262/100,000 in rural and 334-424/100,000 in urban areas. The incidence rate is 119-145/100,000 based on the recent population-based studies. The connection between heart disease and stroke is complex, with shared risk factors, treatments, and outcomes. Additionally, some heart surgeries and medications can unexpectedly lead to neurological issues like ischemic strokes. [21,26].

### 4.3. Congenital Cardiovascular Disease and Kawasaki Disease

Congenital heart disease is a general term for a range of birth defects that affect the normal way the heart works. The term "congenital" means the condition is present from birth. Symptoms of congenital heart disease include rapid heartbeat and breathing, swelling of the legs, tummy or around the eyes, a blue tinge to the eyes. There are many types of congenital heart disease and they sometimes occur in combination. Some of the more common defects include:

1. **Septal defects** – where there's a hole between two of the heart's chambers (commonly referred to as a "hole in the heart").
2. **Coarctation of the aorta** – where the main large artery of the body, called the aorta, is narrower than normal.
3. **Pulmonary valve stenosis** – where the pulmonary valve, which controls the flow of blood out of the lower right chamber of the heart to the lungs, is narrower than normal.
4. **Transposition of the great arteries** – where the pulmonary and aortic valves and the arteries they're connected to have swapped positions.
5. **Underdeveloped heart** – part of the heart doesn't develop properly making it difficult for it to pump enough blood around the body or lungs.

Kawasaki disease causes swelling (inflammation) in the walls of medium-sized arteries throughout the body. Main symptoms include fever, conjunctivitis, skin and mucous membrane affection, and cervical lymphadenopathy. An updated estimation of the national incidence rate for KD is 322 per 100,000 children <5 years. Approximately 85% of affected children with KD are younger than 5 years, although Indian data suggest that almost a third of patients are older. The male to female ratio is approximately 1.5:1. [21,26].

### 4.4. Disorders of Heart Rhythm

A cardiac arrhythmia is a variation from the normal heart rate and/or rhythm that is not physiologically justified. The mechanisms responsible for cardiac arrhythmia are generally divided into 2 major categories: (1) enhanced or abnormal impulse formation (*i.e.*, focal activity) and (2) conduction disturbances (*i.e.*, re-entry). There are several categories of arrhythmia as mentioned below:

- Bradycardia, or a slow heartbeat
- Tachycardia, or a fast heartbeat
- Irregular heartbeat, also known as a flutter or fibrillation
- Early heartbeat or a premature contraction.

Some arrhythmia's do not cause symptoms and are not associated with increased mortality. However, some asymptomatic arrhythmias are associated with adverse events. Examples include a higher risk of blood clotting within the heart and a higher risk of insufficient blood being transported to the heart be-

cause of a weak heartbeat. Other increased risks are of embolization and stroke, heart failure, and sudden cardiac death. If an arrhythmia results in a heartbeat that is too fast, too slow, or too weak to supply the body's needs, this manifests as lower blood pressure and may cause light headedness or dizziness, or syncope (fainting). Some types of arrhythmia result in cardiac arrest, or sudden death [27].

#### **4.5. Sudden Cardiac Arrest, Ventricular Arrhythmias and Inherited Channelopathies**

Sudden cardiac arrest is the abrupt loss of heart function, breathing and consciousness. The condition usually results from a problem with heart's electrical system, which disrupts heart's pumping action and stops blood flow to body. Sudden cardiac arrest isn't the same as a heart attack, when blood flow to a part of the heart is blocked. However, a heart attack can sometimes trigger an electrical disturbance that leads to sudden cardiac arrest [26].

Ventricular tachycardia is a heart rhythm disorder (arrhythmia) caused by abnormal electrical signals in the lower chambers of the heart (ventricles). This condition may also be called V-tach or VT. A healthy heart normally beats about 60 to 100 times a minute at rest. In ventricular tachycardia, the heart beats faster than normal, usually 100 or more beats a minute. The chaotic heartbeats prevent the heart chambers from properly filling with blood. As a result, heart may not be able to pump enough blood to body and lungs. Ventricular tachycardia may last for only a few seconds, or it can last for much longer.<sup>22,23</sup> The person may feel dizzy or short of breath, or have chest pain. Sometimes, ventricular tachycardia can cause the heart to stop (sudden cardiac arrest), which is a life-threatening medical emergency. Many things can cause or contribute to problems with the heart's electrical system. These include abnormalities of the heart that result in scarring of heart tissue (sometimes called "structural heart disease"), poor blood flow to the heart muscle due to coronary artery disease, congenital heart conditions, and imbalance of electrolytes necessary for conducting electrical impulses, use of drugs such as cocaine or methamphetamine [25].

#### **4.6. Subclinical Atherosclerosis**

Atherosclerosis is a chronic, progressive, inflammatory disease with a long asymptomatic phase. Plaque (fatty deposits) build up in arteries is called atherosclerosis. These deposits are made up of cholesterol, fatty substances, cellular waste products, calcium and fibrin (a clotting material in the blood). As plaque builds up, the wall of the blood vessel thickens (Fig. 1). This narrows the channel within the artery – reducing blood flow. That lessens the amount of oxygen and other nutrients reaching the body. This can lead to conditions such as [27, 28, 29].

- Coronary heart disease (plaque in arteries in or leading to the heart)
- Angina (chest pain from reduced blood flow to the heart muscle)
- Carotid artery disease (plaque in neck arteries supplying blood to the brain)
- Peripheral artery disease, or PAD (plaque in arteries of the extremities, especially the legs)
- Chronic kidney disease.

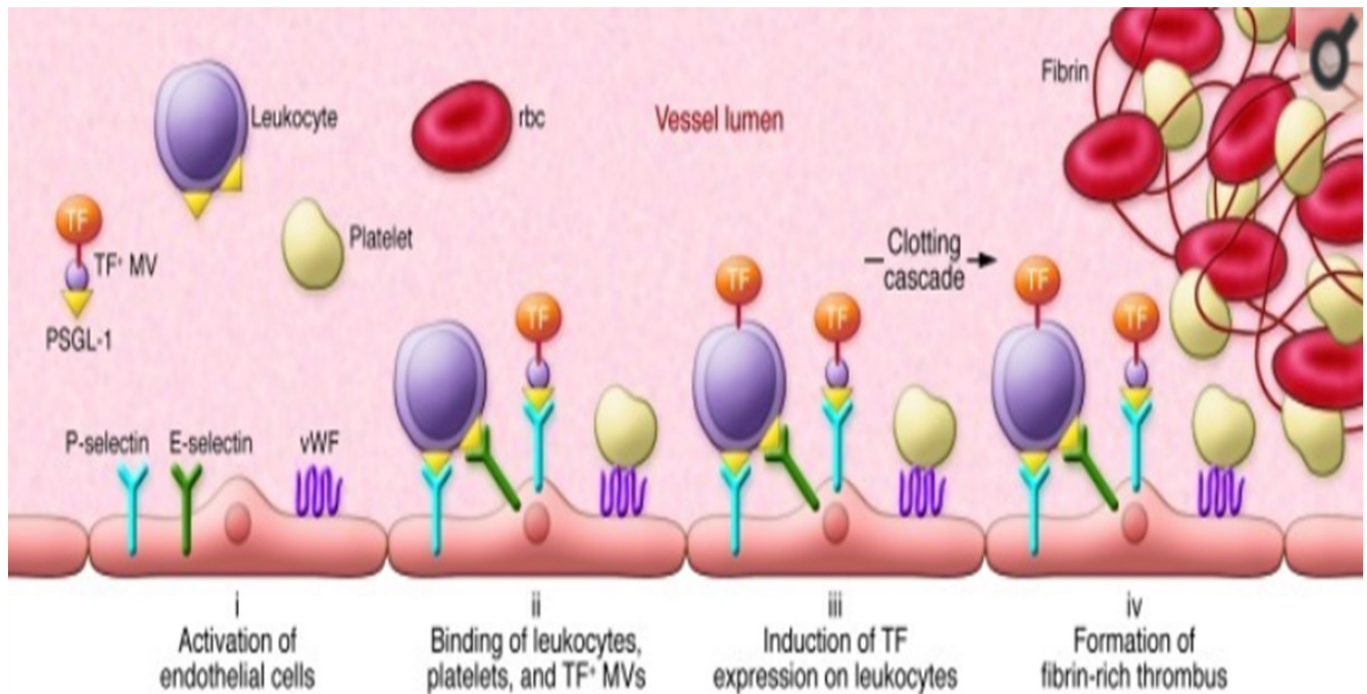
Many scientists believe plaque begins when an artery's inner lining (called the endothelium) becomes damaged. Four possible causes of such damage are:

- Elevated levels of cholesterol and triglycerides in the blood
- High blood pressure
- Cigarette smoking
- Diabetes

#### **4.7. Coronary Heart Disease, Acute Coronary Syndrome and Angina Pectoris**

Coronary artery disease develops when the major blood vessels that supply to heart become damaged or diseased. Cholesterol - containing deposits (plaques) in coronary arteries and inflammation are usually

to blame for coronary artery disease. Coronary artery disease is thought to begin with damage or injury to the inner layer of a coronary artery, sometimes as early as childhood. The damage may be caused by various factors, including smoking, high blood pressure, high cholesterol, diabetes or insulin resistance and not being active (sedentary lifestyle) [30,31].



**Fig. (1).** Formation of thrombosis in the lumen of blood vessel, the aggregation of different circulating factors, adhering to the luminal wall narrowing the passage.

Angina, also known as angina pectoris, is chest pain or pressure, usually due to insufficient blood flow to the heart muscle. Angina is usually due to obstruction or spasm of the arteries that supply blood to the heart muscle. Other causes include anaemia, abnormal heart rhythms, and heart failure. The main mechanism of coronary artery obstruction is atherosclerosis as part of coronary artery disease. Angina usually happens because of heart disease. A fatty substance called plaque builds up in your arteries, blocking blood flow to heart muscle. This forces heart to work with less oxygen that causes pain. The person may also have blood clots in the arteries of heart, which can cause heart attacks. Certain lifestyle habits could put an individual at higher risk of angina, including older age, family history of heart disease, high cholesterol, diabetes, obesity, stress, using tobacco and physical inactivity [31,32,33].

#### 4.8. Cardiomyopathy and Heart Failure

Heart failure is the inability of the heart to provide sufficient blood flow to meet the needs of the body for oxygenated blood during regular activity or to do so only with elevated pressures within the heart. It can occur when the heart muscle is weak (systolic failure) or when it is stiff and unable to relax normally (diastolic failure). Cardiomyopathy, which means “disease of the heart muscle,” is one of many causes of heart failure. In the adult population over age 20, the prevalence of heart failure is 2.6 percent. It is generally higher in men than in women but highest in black women [34].

In cardiomyopathy, the heart muscle becomes enlarged, thick, or rigid. In rare cases, the muscle tissue in the heart is replaced with scar tissue. As cardiomyopathy worsens, the heart becomes weaker. It is less able to pump blood through the body and maintain a normal electrical rhythm. This can lead to heart failure or irregular heartbeats called arrhythmias. Heart failure can cause fluid to build up in the lungs, ankles, feet, legs, or abdomen. The weakening of the heart also can cause other complications, such as heart valve problems. The types of cardiomyopathy are: [35].



- Hypertrophic cardiomyopathy
- Dilated cardiomyopathy
- Restrictive cardiomyopathy
- Arrhythmogenic right ventricular dysplasia
- Unclassified cardiomyopathy.

Cardiomyopathy can be acquired or inherited. “Acquired” means an individual isn’t born with the disease, but develops it due to another disease, condition, or factor. “Inherited” means parents passed the gene for the disease on to children. The primary pathophysiological mechanisms implicated in cardiomyopathy include defective force generation caused by mutations in sarcomere protein genes; defective force transmission caused by mutations in cytoskeletal protein genes; myocardial energy deficits caused by mutations in both nuclear and mitochondrial DNA encoded genes; and abnormal  $Ca^{++}$  homeostasis caused by altered availability of  $Ca^{++}$  and altered myofibrillar  $Ca^{++}$  sensitivity [35,36].

#### **4.9. Valvular Diseases**

Valvular heart disease is any cardiovascular disease process involving one or more of the four valves of the heart (the aortic and mitral valves on the left side of heart and the pulmonic and tricuspid valves on the right side of heart). These conditions occur largely as a consequence of ageing but may also be the result of congenital (inborn) abnormalities or specific disease or physiologic processes including rheumatic heart disease and pregnancy. Valve failure or dysfunction can result in diminished heart functionality. Valvular heart disease can be caused by valvular stenosis or valvular insufficiency. In the valvular heart disease condition valvular stenosis, the tissues forming the valve leaflets become stiffer, narrowing the valve opening and reducing the amount of blood that can flow through it. If the narrowing is mild, the overall functioning of the heart may not be reduced. However, the valve can become so narrow (stenosis) that heart function is reduced, and the rest of the body may not receive adequate blood flow. Another valvular heart disease condition, called valvular insufficiency (or regurgitation, incompetence, "leaky valve") occurs when the leaflets do not close completely, letting blood leak backward across the valve. This backward flow is referred to as “regurgitated flow.” Bicuspid aortic valve disease is a type of congenital valve disease that affects the aortic valve. The valve has two leaflets (cusps) instead of three. Without the third leaflet, the valve may be: [37,38].

- Stenosis - stiff valve leaflets that cannot open or close properly
- Leaky - not able close tightly (regurgitates).

#### **4.10. Venous Thromboembolism (Deep Vein Thrombosis and Pulmonary Embolism), Chronic Venous Insufficiency, Pulmonary Hypertension**

Venous thromboembolism (VTE) is a disorder that includes deep vein thrombosis and pulmonary embolism. A deep vein thrombosis (DVT) occurs when a blood clot forms in a deep vein, usually in the lower leg, thigh, or pelvis. A pulmonary embolism (PE) occurs when a clot breaks loose and travels through the bloodstream to the lungs Fig. (1). Swelling, redness, and pain are some of the signs and symptoms of deep vein thrombosis. A pulmonary embolism can cause sudden chest pain and shortness of breath. VTE occurs in the veins that carry blood to the heart. A deep vein thrombosis may occur if the flow of blood slows down in body’s deep veins, if something damages the blood vessel lining, or if the makeup of the blood itself changes so that blood clots form more easily. A pulmonary embolism (PE) refers to an embolus from a deep vein blood clot that breaks loose and travels to the lungs, blocking an artery in the lung. Blood clots can develop in veins damaged by surgery or trauma, or a result of inflammation in response to an infection or injury. Some conditions are more closely linked to developing VTE and include spinal cord injury, a broken hip or leg bone or other trauma, cancers, heart conditions such as heart attack or congestive heart failure, stroke, obesity, varicose veins, sickle cell disease. Without treatment, pulmonary embolism is associated with a mortality rate of approximately 30%, causing nearly 50,000 deaths per

year. The most common forms of occlusive thrombosis occur in arteries and lead to myocardial infarction and stroke. Deep vein thrombosis (DVT) mostly occurs in the legs and is associated with pulmonary embolism (PE); collectively, these are termed venous thromboembolism (VTE) [36,37,38,39].

Chronic venous insufficiency (CVI) is a common but under diagnosed cause of leg pain and swelling, and it is frequently associated with varicose veins. It is a consequence of the dysfunction of the valve of the veins, associated with an impaired circulation of blood in the leg veins. Valve failure may occur due to a weakening of the valves as a result of varicose veins, or damage to the deep veins secondary to venous thrombosis, trauma or venous obstruction. The failure of the valves allows the blood to flow back down (reflux) into the section of vein below. This prevents the reduction in venous pressure that normally occurs during exercise, resulting in venous hypertension. In addition, poor function or failure of the calf muscle pump due to inactivity, immobility or abnormal gait may contribute to venous hypertension. Risk factors for CVI are family history, increasing age over 30, one or more blood clots in superficial or deep veins, female gender; varicose veins occur nearly as commonly in men, prolonged standing, heavy lifting, multiple pregnancies, limited physical activity, high blood pressure and obesity [39,40].

Pulmonary hypertension is defined as resting mean pulmonary artery pressure of  $\geq 25$  mm Hg. Pulmonary hypertension happens when the pressure in the blood vessels leading from the heart to the lungs is too high. With pulmonary hypertension, the blood vessels to the lungs develop an increased amount of muscle in the wall of the blood vessels. The heart pumps blood from the right ventricle to the lungs to get oxygen. Because the blood does not have to travel very far, the pressure in this side of the heart and in the artery taking blood from the right ventricle to the lungs is normally low—usually much lower than systolic or diastolic blood pressure. When the pressure in this artery gets too high, the arteries in the lungs can narrow and then the blood does not flow as well as it should, resulting in less oxygen in the blood [25,37].

#### 4.11. Peripheral Artery Disease and Aortic Diseases

Peripheral artery disease (also called peripheral arterial disease) is a common circulatory problem in which narrowed arteries reduce blood flow to your limbs. When a person develops peripheral artery disease (PAD), the legs or arms usually don't receive enough blood flow to keep up with demand. This may cause symptoms, such as leg pain when walking (claudication). Peripheral artery disease is also likely to be a sign of a build up of fatty deposits in the arteries (atherosclerosis). This condition may narrow arteries and reduce blood flow to legs and, occasionally, to arms. Claudication symptoms include muscle pain or cramping in your legs or arms that's triggered by activity, such as walking, but disappears after a few minutes of rest. The location of the pain depends on the location of the clogged or narrowed artery. Calf pain is the most common location [27,38].

Aortic disease: The aorta is the largest artery in the body. Oxygen-rich blood enters the aorta and the heart pumps the blood out of the aorta where it travels to the rest of the body *via* the smaller arteries that branch out from it. When affected by disease, the aorta can split (dissection) or dilate (aneurysm) and in either case, the rupture may have fatal results. Three types of aortic aneurysms can be classified as:

- Abdominal aortic aneurysms
- Thoracic aneurysms
- Thoracic abdominal aneurysms

An abdominal aortic aneurysm is an enlarged area in the lower part of the major vessel that supplies blood to the body (aorta). The aorta runs from heart through the Center of chest and abdomen. It is the largest blood vessel in the body, so a ruptured abdominal aortic aneurysm can cause life-threatening bleeding [33,34].

A thoracic aortic aneurysm is a weakened area in the major blood vessel that feeds blood to the body (aorta). When the aorta is weak, blood pushing against the vessel wall can cause it to bulge like a balloon (aneurysm). A thoracic aortic aneurysm is also called a thoracic aneurysm, and aortic dissection can occur because of an aneurysm. A dissection is a tear in the wall of the aorta that can cause life-threatening bleed-

ing or sudden death. Large, fast-growing aneurysms also may rupture, but small and slow-growing aneurysms may never rupture [34,37].

A thoracoabdominal aortic aneurysm is a bulging in the aorta that extends from the chest to the abdomen. The most common cause of thoracoabdominal aortic aneurysms is atherosclerosis which is a hardening of the arteries caused by plaque build-up. Over time, this plaque can cause the walls of the aorta to become stiff and weak, creating the potential for an aneurysm to form.

#### 4.12. Genetics

Many cardiac disorders can be inherited, including arrhythmias, congenital heart disease, cardiomyopathy and high blood cholesterol. Coronary artery disease leading to heart attack, stroke, and heart failure can run in families, indicating inherited genetic risk factors. Genetics can influence the risk for heart disease in many ways. Genes control every aspect of the cardiovascular system, from the strength of the blood vessels to the way cells in the heart communicate. A genetic variation (mutation) in a single gene can affect the likelihood of developing heart disease. Genetic factors likely play some role in high blood pressure, heart disease, and other related conditions. However, it is also likely that people with a family history of heart disease share common environments and other factors that may increase their risk. The risk for heart disease can increase even more when heredity combines with unhealthy lifestyle choices, such as smoking cigarettes and eating an unhealthy diet. The scientists combined all their data and came up with six genetic variants that were linked to heart attacks or heart disease. Those variants are in or near the *MTHFD1L*, *PSRC1*, *MIA3*, *SMAD3*, *CDKN2A/CDKN2B*, and *CXCL12* genes [33].

### 5. OUTCOMES

#### 4.1. Quality of Care

The Institute of Medicine defines quality of care as “the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge,” identifying 6 specific domains for improving health care: safety, effectiveness, patient- or people-centeredness, timeliness, efficiency, and equity. In 119,735 patients with acute myocardial infarction who were admitted to 1824 hospitals, Bucholz and colleagues showed that patients admitted to high-performing hospitals after acute myocardial infarction had longer life expectancies than patients treated at low-performing hospitals. This signal appeared in the first 30 days and persisted over 17 years of follow-up. Patients treated at high-performing hospitals lived on average 0.74 to 1.14 years longer than patients treated at low-performing hospitals. Lower-volume hospitals were significantly less likely to be adherent to heart failure process measures than higher-volume hospitals. In a longitudinal cohort study of 48 million hospitalizations among 20 million Medicare fee-for-service patients across 3497 hospitals, Desai and colleagues showed that patients at hospitals subject to penalties under the HRRP had greater reductions in readmission rates than those at non-penalized hospitals. A study of 2083 patients with ischemic stroke from 82 hospitals with data in both the AVAIL registry and GWTG-Stroke found that one-third of patients with acute stroke were functionally dependent or dead at 3 months after stroke. Functional rates varied considerably across hospitals indicating the need to understand which process measures could be targeted to minimize hospital variation and to improve post stroke functional outcomes [40,42].

#### 5.2. Medical Procedures

- **Coronary Artery Bypass Grafting:** In 1997, the number of inpatient discharges for CABG was 484 000 for males and 199 000 for females. These numbers declined to 276,000 and 94,000 respectively, in 2014 [40,41,42,43].
- **Inpatient Cardiac Catheterization and PCI:** Inpatient PCI discharges decreased from 359,000 for males and 190,000 for female in 1997 to 325,000 and 155,000, respectively, by 2014. From 2004 to 2014, the number of inpatient cardiac catheterizations decreased from 1,486,000 to 1,016,000 annually [42].

- **Cardiac Open-Heart Surgery:** Among other major procedures in 2016, there were 28493 isolated aortic valve replacements and 7706 isolated mitral valve replacements; 17 507 procedures involved both aortic valve replacement and CABG, whereas 2935 procedures involved both mitral valve replacement and CABG [43].
- **Heart Transplantations:** Of the recipients in 2019, 69.5% were male, 61.2% were White, 22.4% were Black, 11.2% were Hispanic, and 3.5% were Asian. For transplantations that occurred between 2008 and 2015, the 1-year survival rate was 90.5% for males and 91.1% for females; the 5-year survival rates based on 2008 to 2015 transplantations were 78.4% for males and 77.7% for females. The 1- and 5-year survival rates for White patients undergoing cardiac transplantation were 90.7% and 79.1%, respectively. For Black patients, they were 90.7% and 74.1%, respectively. For Hispanic patients, they were 90.1% and 80.0%, respectively. For Asian patients, they were 91.4% and 80.1% [43].

## 6. ECONOMIC COST OF CARDIOVASCULAR DISEASE

The direct economic burden of heart disease in India could be 200 billion rupees (\$ 4.5 billion). This would increase to 800 billion rupees (\$ 18 billion) if 100% of the CAD patients were aware and received necessary treatment. Indirect costs would make the numbers even higher. The economic burden of CVD varies among states with Kerala amounting to as much as 20% of its state domestic product. Modelling studies have shown that the per capita real GDP in India would grow by an additional 87% from the year 2000 per capita GDP if the annual CVD mortality declines by 1%, whereas a 3% annual decline in CVD mortality would increase per capita income by 218% by the year 2030. India had the highest 15-month out-of-pocket CVD expenditures where the median income was INT (International Dollars) \$259/month and only 16% of the respondents had insurance coverage. The combined inpatient and outpatient services CVD expenditure ranged from INT \$773 in low-income to \$1593 in middle income and \$2917 in high income Indians, whereas the median individual monthly income was \$136, \$181 and \$302 respectively. The household median income was INT \$212, INT \$302 and INT \$665 respectively. Thus, the average out-of-pocket CVD expenditure was the equivalent of >6-month salary for all income groups. Heart disease is a silent disease with 75% of the patients being unaware of the presence of the disease. Therefore, only 25% would receive any kind of treatment (statins, aspirin, beta blockers, hospitalization, thrombolytic therapy, angioplasty, stent, and bypass). The WHO (World Health Organization) has estimated that a 2% annual reduction in national-level chronic disease death rates in India would result in an economic gain of USD 15 billion for the country over the next 10years. More than 80% of the population pays out of pocket for healthcare expenditure. As a result, 30 million are pushed into poverty every year [42,43,45].

## CONCLUSION

Stroke remains a significant health issue, impacting countless individuals globally each year. This review emphasizes the crucial role of early detection and prompt intervention in improving patient outcomes. Breakthroughs in imaging technology and the identification of biomarkers are transforming stroke diagnosis and treatment, paving the way for more targeted and effective therapies. However, numerous challenges persist. Inequities in access to stroke care and treatment outcomes point to the urgent need for more inclusive and fair healthcare systems.

Looking to the future, personalized medicine represents a promising frontier in stroke care. By customizing treatments based on each patient's unique genetic and clinical characteristics, we can enhance the efficacy of interventions. Continued research into new therapeutic targets is also vital. Furthermore, there must be an increased focus on comprehensive post-stroke care and rehabilitation, as these are critical for the recovery and overall quality of life of stroke survivors. Ultimately, reducing the global impact of stroke requires a united effort. Collaboration among healthcare professionals, researchers, and policymakers is essential to foster innovation in stroke prevention, diagnosis, and treatment. Through these collective efforts, we can make significant progress in improving the lives of those affected by stroke, aiming towards a future where stroke is no longer a major cause of disability and mortality.

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The author confirms sole responsibility for the following: study conception and design, data collection, analysis and interpretation of results, and manuscript preparation.

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