

Cardio Vascular Disease – An Epidemiological review

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ABSTRACT

Over a decade, world was dominated by malnutrition such as pellagra, rickets, etc.; communicable diseases such as hepatitis, Cholera, etc.; which was responsible for higher morbidity and mortality rates at rapid pace. In the recent years, as the mortality rates climbed up in the developing countries due to major turn-around from malnutrition, communicable diseases to non-communicable diseases (NCD): "*Epidemiological Transition*". Global Burden of Disease (GBD) study, reported that mortality rates resulting from NCD's have increased due to improvisation in socio-economic status, changes in demographic, ecological and natural production of medicinal drugs. The NCD's comprises a spectrum of disorders and risk factors. Among the NCD's, cardiovascular diseases (CVD) emerged as most vital, burden diseases among low-income, developing countries & western countries. In the broad spectrum of CVD, atherosclerosis is a major cause for cardiovascular morbidity and mortality. Atherosclerosis is characterized by extreme inflammation and accumulation of lipids in blood vessels which subsequently leads to further clinical complications. In this review, we discuss the recent epidemiological transition facts about atherosclerosis, which will provide a better perceptible about CVD.

Key Words: Communicable Diseases, Non Communicable Diseases, Cardiovascular diseases, Atherosclerosis.

INTRODUCTION

Disasters like flood, hurricanes, drought resulted in immense outbreak of diseases and economic crisis in developing and low income countries. These outbreaks of disease and economic crisis ultimately ruined into increased mortality rates especially through communicable diseases. In 1950, the anticipation about life at birth was around 46 years, but similar probability got improved to 66 years at 1980¹. This anticipation sets up a platform and witnesses the major turn-around in the pattern of diseases. At present the world population is undergoing a massive demographic transition, which has resulted in a rapid increase of NCD replacing the other pre-existing disorders such as communicable diseases, malnutrition, etc.². NCD provoke a daunting task as it affects more number of cases in developing countries compared to high income countries in the preliminary phase of the economic development. CVD is considered to be dreadful in the trend of NCD. As vascular system delivers to vital organs such as brain, heart; any changes in vascular network will affect the function of organs³. It proved to be the primary cause for mortality globally^{4,5}. Nearly 50% and 28% of deaths in high yield & low yield income countries respectively resulted due to CVD⁶. Three reasons may be anticipated for the rise of CVD; socio-economic changes, physical inactivity and

susceptible populations. In the developing countries, hyperlipidemia was responsible for majority of CVD deaths^{7,8}. In addition people have metabolic syndrome like obesity, hypertension, and diabetes mellitus (DM) which makes them more vulnerable to CVD.

Cardio Vascular Disease and its various forms

The term "Cardiovascular Diseases" (Cardio from *Greek kardia* - Heart; Vascular, from *Latin vasculum* - Little vessel) generally stands for a group of disorders which involves heart and blood vessels. CVD is normally accompanied by two or more diseases due to various risk factors referred as *co-morbidity*. For example smoking, alcohol consumption results in Coronary Artery Diseases (CAD), chronic kidney disorder, stroke, cancer, respiratory diseases, and diabetes mellitus. Majority of CVD is triggered up on by common risk factors such as smoking, hypertension and obesity. Irrespective of the age and sex, these risk factors provide major contribution for the development of broad series of CVD, which as follows,

1. Coronary Artery diseases (CAD)

CAD is characterized by narrowing of blood vessels supplying to the heart muscle due to plaque formation. Plaque is composed of macrophages, foam cells, cholesterol, and fatty deposits.

Hypertension, diabetes, dyslipidemia, stress, smoking are the leading risk factors for the progression of CAD. It often leads to two clinical states namely Heart attack (Myocardial Infarction) and Angina. In myocardial infarction blood vessels supplies to heart will be suddenly get blocked and resulting in an insult to heart muscle. In angina, chest pain occurs at regular interval whenever heart undergoes inadequate blood supply.

2. Cerebrovascular diseases

Cerebrovascular diseases affect the distribution of blood supply to brain, and eventually results in brain dysfunction. Blood supply demand of the brain, when it is not met, this imbalance will cause brain deficit such as ischemic stroke, hemorrhagic stroke. The most commonly occurring forms of cerebrovascular diseases are cerebral thrombosis and cerebral embolism. Risk factors such as serum cholesterol, fibrinogen, high blood pressure, ethnicity, alcohol consumption, diet, and smoking contribute for the development of cerebrovascular diseases. The ratio of death due to CVD to cerebrovascular disease will be 4:1. Out of every 4 deaths in CVD, 1 of deaths would be due to cerebrovascular disease.

3. Hypertension

The term Hypertension is commonly referred to as high blood pressure; is of two type's namely Primary and secondary hypertension. Primary hypertension has no specific causative; it has 95% prevalence rate. It affects the brain, kidneys, eyes and blood vessels. Secondary hypertension caused by endocrine diseases etc., It has 5-10 % prevalence rate. Increase in blood pressure will result in twofold increase of the risk of stroke and heart attack. Mental stress, smoking, and diabetes mellitus are the major risk factors for the hypertension.

4. Peripheral vascular disease (PVD)

'PVD' is characterized by the deposition of atheroma in the wall of the blood vessels especially that supplies blood to the arms and the legs. The prevalence rate is around 12-14%. It results from various disorders like atherosclerosis, DM, obesity (BMI>30), high blood pressure, high cholesterol; advanced age and smoking, physical inactivity are prone to be responsible for the development of peripheral vascular disease.

5. Rheumatic heart disease

Rheumatic heart disease is the damage of the heart muscle and valves as a result of acute rheumatic fever (caused by *Streptococcus pyogenes*). The prevalence rates lies around 12.4%. In the childhood, affected population will have an abnormal immune responses developed against streptococcal infection, which will automatically

lead to valvular damages. Children in the age group of 5-14 yrs are more vulnerable to rheumatic fever. It manifests as a combination of fever, carditis, and chorea, lesions in skin, polyarthritis and subcutaneous nodules. Poor sanitation and poverty are the root cause of bacterial infections and results in rheumatic heart disease.

6. Heart failure

Heart failure is characterized when the heart is unable to maintain sufficient amount of blood flow to the body requirement. Diabetes, CAD and hypertension are prone to be responsible for heart failure. It is broadly classified into class I, II (Mild), III (Moderate) and IV (Severe) stages of heart failure. Heart attack, hypertension, cardiomyopathy will further pave way for the additional overload to the heart, and finally leads to heart failure. Smoking, alcohol consumption, diabetes and obesity lead the table of risk factors leading to heart failure.

7. Deep vein thrombosis

Deep vein thrombosis "DVT" is characterized by formation of blood clots in the large veins of the leg or pelvic region, which can dislodge to the heart and lungs. The presence of blood clot in leg carries less threat, than on it dislodges to other organs. It creates serious threat to life as the blood clot takes place in "deep vein". Risk factors like severe fracture in the hip, spinal cord injury, hormone replacement therapy, obesity, frequent travel will leads in deep vein thrombosis.

8. Congenital heart disease

Congenital heart disease is a deformity of heart structure that gets manifests at birth. It carries higher mortality in the preliminary period of infant age. It is characterized by reduced blood flow and is usually portrayed by abnormalities in heart valves such as the valve incompetency (stenosis /regurgitation). It often classified as cyanotic (skin changes into blue color due to insufficient supply of oxygen) and non-cyanotic congenital heart disease. Maternal diabetes mellitus, Noonan syndrome, Down syndrome and maternal infection pose a major threat in terms of risk factors for the progression of congenital heart disease. Among every 1000 newborns, congenital heart disease occurs at 8 newborns.

Risk Factors – Cardiovascular disease

The epidemiological transition ended in a major outbreak of cardiovascular diseases. This revolution influenced by various factors including Socio-economic problems, dietary changes, life style etc. World Health Organization had identified major risk factors comprises minimum of 20 risk factors, which are responsible for major casualties in Global Burden Diseases including

cardiovascular diseases. 47% of premature deaths and 39% of total burden diseases are resulted due to combined risk factors effects⁹. The existence of risk factors for longer period of time increases the risk of onset of diseases at any time. But extent of the risk factors and their role in virulence is entirely depending on age and sex factor. In CVD, risk factors commonly fall under two categories namely modifiable risk factors and non modifiable risk factors.

➤ **Modifiable risk factors**

The factors can be controlled through human intervention, thereby reducing the probability of disease. It includes increased tobacco usage, high blood pressure, abnormal lipid levels, increased alcohol consumption, low socio-economic status, increased stress, unhealthy diets, physical inactivity, DM, hyperlipidemia, increased obesity.

➤ **Non-Modifiable risk factors**

The risk factors occur irrespective of any changes in the society or any environmental impacts. It comprises advanced age, heredity or family history, ethnicity or race, gender.

In cardiovascular disease, modifiable risk factors play a predominant role in the progression and ends in mortality. Based on geographical locations the risk factors also differs (Table 1)¹⁰.

Trends in Epidemiological Transition in allied to CVD

Industrial and technological revolutions; socio-economic transformations had resulted in the dramatic turnaround in the mortality from infectious diseases & malnutrition to cardiovascular disease. Better accessibility of food, improved hygiene, easy affordability of antibodies & vaccines lead to increased life span, which eventually leads to the greater prevalence of CVD. The time duration of manmade or artificially invented degenerative disease is portrayed by various life style changes that includes physical activity, smoking, dietary changes wherein these changes typically lay the platform for the arrival or materialization of atherosclerosis. In CVD, the mortality rate surpassed when compared to that of the mortality rates occurring due to other infectious diseases¹¹. In the beginning of the 20th century, CVD was known to be causative and also responsible for 10% of overall death globally. But at present the mortality rates have increased by 30% due to CVD^{12,13}.

Cardiovascular disease - Resolutions & Certification

1. The mounting burden of cardiovascular diseases was first universally recognized during at the 1st **International declaration on CVD** at 1956¹⁴.

2. In 1956, India anticipated a resolution on CVD and Hypertension in the 9th **World Health Assembly**¹⁴.
3. At 1984, **World Bank** published the report regard increasing trouble of CVD exists among the Chinese populations¹⁵.
4. In 1992, **The Victoria Declaration on Heart Health** provoked the logic of necessity for the prevention and control measures of the CVD for the first time¹⁶.
5. In 1993, **World Bank** published the 1st pamphlet on emphasizing the universal burden of CVD¹⁷.
6. In 1993, **World Bank World Development** reported the urgency of investing in public health through Government agencies among Low- income and Developing countries¹⁷.
7. In 1993, **World Development report** published Disease Control Priorities (DCP) in Developing Countries, which stressed the need of measurement and intervention of diseases¹⁸⁻²⁰.
8. In 1995, **The Catalonia Declaration**, brought the revolution in prevention of CVD through awareness programs and policies^(21,22).
9. In 1997, **The Singapore Declaration** briefed how to develop the infrastructure for Heart health at local, National and international level²³.
10. In 1998, Institute of Medicine (**IOM**) explained the necessary of establishing and investing in the R & D to tackle the CVD²⁴.
11. At 1999, **Director General, WHO** submitted put up a strategy to deal with prevention of Non Communicable Diseases. In due course of time it sets a tone for the future WHO strategies²⁵.
12. In 2000, **Victoria Declaration** emphasized Women are more susceptible to CVD and called for government, Non- Governmental Organizations to invest in awareness programs of CVD for the women upliftment²⁶.
13. In 2001, **The Osaka Declaration** briefed the role of socio-economic, political factors behind the lack of progress in creating awareness on CVD²⁷.
14. In 2001, **WHO's Assessment of National Capacity for Noncommunicable Disease** report, gave a node to identify and provide the technical support in selected regions universally to battle the NCD²⁸.
15. In 2002, **WHO** report made a framework to visualize the risk factors in relation to healthy life²⁹.
16. In 2003, **World Health Assembly** prepared a treaty to reduce the usage of Tobacco by imposing tax, social measures, price, and regulations³⁰.

17. In 2003, 7th **Joint National Committee** reports highlighted the risk threshold and principles of hypertension in adults³¹.
18. In 2004, **WHO** drafted the policy on Diet, Physical activity & health. It facilitates to realize the influence of diet and physical activity on healthy life in the world Population³².
19. In 2004, **Milan declaration** underlined the responsibility of informational technology, Communicational technology, food technology, medical biotechnology in reduction of cardiovascular diseases³³.
20. In 2004, **Earth Institute** reported statistical data on Socio-economic impacts of CVD on present and future aspects³⁴.
21. In 2005, **Lancet** published series of articles highlighting the concept of global health in relation to chronic disease³⁵.
22. In 2008, **The Oxford Alliance Summit** passed the Sydney Resolution & Sydney Challenge to seize an action against the preventable chronic diseases³⁶.
23. In 2008, **Global Burden of Disease** stated out of 10 deaths globally, 6 are due to NCD³⁷.
24. In 2009, **IOM** report identified the United States of America involved in global health concerns and also highlights the increasing trends of NCD in low and middle income countries³⁸.

These documentation and amendments facilitate to realize the serious impacts of CVD globally.

A Glance about Atherosclerosis

It took around 500 years for us to realize about the existence of atherosclerosis, presently known as a lethal disorder. The role of pathology in atherosclerosis was recorded 150 years ago. Recently around 25 years ago the role of vascular biology in atherosclerosis was identified³⁹. Incrustation hypothesis on atherosclerosis conquered the fields of epidemiology, human physiology, and clinical studies on CVD in the 2nd half of last century. The term Atherosclerosis refers to "*Athere- Gruel* or Accumulation of Lipids and *Sclerosis* – Hardening. It also described as Arteriosclerotic Vascular disease (ASVD) (Table 2). In the recent years atherosclerosis has emerged one of the most prominent causative disorders resulting in the higher number of mortality. Atherosclerosis more frequently entitled as multifactorial diseases is the passage spot between genetic and environmental factors⁴⁰.

The proclivity for the development of this disease was seen more in men than in women as an outcome of the changes in dietary habits, smoking, physical and mental stress⁴¹. These factors are responsible for the abnormalities to be transpired into multiple tissue and various types of cell, which eventually results in the development of

cardiovascular diseases⁴². Atherosclerosis is not only a disorder, but it is a foremost donor that leads to the pathogenesis, loss of function in nearby components. It will not develop straightaway in the adult stage as an atherosclerotic plaque; but it forms as fatty streaks in the human fetus, during the condition of maternal hypercholesterolemia at the pregnancy stage⁴³. It apparently leads into further clinical complications like coronary CHD, PVD.

Plaque Formation in Atherosclerosis

Atherosclerosis is commonly witnessed by plaque formation. Plaque is a fatty substance, which gets deposited up in the walls of arteries. Deposition of fatty substance results in thickening of arteries and loss of flexibility. Plaque formation not only affects the nature of arteries, but it also constricts the blood flow in the arteries (Figure 1). Further complication of plaque is development of blood clots within the arteries, which in turn causes sudden blockage of blood flow in & out of artery. Plaque occurs in two forms either as hard or stable and soft or unstable. Stable plaque causes thickening of artery walls, while the unstable plaque causes blood clots.

From the earlier hypothesis, atherosclerosis is often referred as lipid storage diseases, but the recent view indicates it as an inflammatory disease. This inflammatory condition is usually characterized by macrophage cells, foam cells, smooth muscle cells, platelets, growth factors etc.,. Depending on accumulation of different cells, occurrence either at adults or birth the atherosclerotic lesions is classified as following types.

Type I lesion

- Type 1 most commonly occurs in infants and children.
- It also referred as "Initial lesion" as it occurs in the early stage of lesion formation.
- In the preliminary stage it contains minute lipid deposits in the intima.
- In the infants it occurs as yellow spots and cannot be studied by naked eye.
- In the later stage accumulation of lipoprotein, increase in macrophages, development of foam cells takes place.

Type II lesion

- It is characterised by presence of "Fatty streaks" and materialized as yellow streaks or spots or patches.
- It is also called as "Sudanophilic lesion" as it is stained with Sudan III or IV stain.
- In the initial stage of type 2 lesion macrophage cells are arranged in the flanking layers.
- It contains huge numbers of macrophage cells and meager numbers of T lymphocytes.

- Also characterized by the presence of macrophage foam cells, endothelial cells, and smooth muscle cells.
- Lipid of Lesions II is composed of cholesterol esters, cholesterol, and phospholipids.
- Lesions II are visible to unaided or naked eye.

Type III lesion

- It is also identified as the intermediate lesion.
- Type III lesion exhibits a morphological & chemical bridge linking type II lesion and type IV lesion.
- The lipid droplets may either be membrane bounded or freely available.
- It is composed of free cholesterol, fatty acid, sphingomyelin, lysolecithin, and triglyceride.

Type IV lesion

- It is characterized by intense buildup of extracellular lipid; arrangement referred as "lipid core".
- Type IV is lesion considered as advanced one among the three lesions because of severe intima disorganization due to lipid core.
- It also has macrophages, smooth muscle cells, lymphocytes and mast cells.
- Type IV lesion are susceptible to rupture due to the presence of densely populated macrophages.
- It results in mortality due to severe disorganization of intima.

Type V lesion

- It is more commonly characterised by formation of new fibrous connective tissues, which is densely populated.
- Type V lesion is classified into three subtypes, namely Type Va, Type Vb & Type Vc.
- Type Va or fibroatheroma, usually referred to when new fibrous connective tissue is attached with lipid core.
- Type Vb usually refers to when lipid cores and other regions of lesions are calcified.
- Type Vc usually refers to when the lipid core is absent.
- Fibrous connective tissue is mostly responsible for the thickness of the lesions.
- It is symbolized by the presence of increased amount of collagen, smooth muscle cells.
- Mortality in atherosclerosis is chiefly due Type IV and V lesions.

Type VI lesion

- Also referred as "Complicated lesions".
- It is classified into three types namely, Type VIa, VIb, VIc and VIabc
- Type VIa consists of Surface rupture, VIb consists of hemorrhage or hematoma and VIc consists of thrombosis; VIabc consists of Rupture, hemorrhage and thrombosis.
- Type VI lesions are known to be with the presence of bulges or aneurysms which results in increased erosion of intimal surface.

Risk factors – Atherosclerosis

Atherosclerosis, a complex disease often involves mechanism of the vascular, metabolic, and immune systems. Risk factors are generally categorized into modifiable, non-modifiable based on their impacts.

Modifiable risk factors

Low-density lipoproteins (LDL)

The sequence of atherosclerotic plaque formation is considered to begin with accumulation of LDL. Various studies have justified that elevated levels of LDL are known to be causative for the occurrence of CHD, which directed National Cholesterol Education Program (NCEP), to consider LDL as a major atherogenic lipoprotein⁴⁴. Virulence of LDL differs in terms of size; National Cholesterol Education Program Adult Treatment Panel III had agreed that small LDL possess major threat in the development of CVD⁴⁵. Arterial tissue makes the way for entry of small, opaque LDL rather than larger LDL due to the property of transendothelial convey of minor particles. But there is midst of disarray prevails regarding the association of LDL size and levels for the advancement of CHD. The oxidation of LDL can also provoke the development of atherosclerosis, which is confirmed by its presence in subclinical atherosclerotic conditions. Through therapeutic inflection, it is possible to dethrone the threat of LDL from progressing into CHD.

High-density lipoproteins (HDL)

The decreased levels of HDL are alleged to be one of risk factors for CHD. Various clinical studies and surveys authenticated the levels of HDL are inversely associated with the risk of CHD^{46,47}. HDL plays a crucial role in reverse cholesterol transport (RCT), which removes excess cholesterol from the peripheral tissues and sends back to liver for catabolism. A decreased level of HDL affects the RCT pathway, which in turn results in atherosclerosis, as accumulation of cholesterol takes place in peripheral tissues. Decreased level of HDL also fails to protect the endothelial cells from tumor necrosis factor – α ; As TNF- α desirably leads to atherosclerosis⁴⁸.

Diabetes mellitus (DM)

Among the list of risk factors, DM more predominantly occupies its position for increased mortality rate. People already having DM are prone to two to four fold higher risk of developing CVD. DM occurs in two forms namely Type 1 & Type 2; among these, Type 2 diabetes mellitus closely associated and well known risk factor for CHD⁴⁹. Majority of DM patients have increased LDL level and decreased HDL levels, which promotes the rate of CHD. Recent studies, reveals patients with impaired fasting glucose (IFG) have higher possibilities for advancement into CHD⁵⁰.

Smoking

In CVD, one- third of death results due to smoking and tobacco use. Risk of CVD due to smoking can be analyzed, depending on following parameters: duration of smoking, extent of inhalation, usage of cigarette etc., As a result of smoking, nicotine stimulates the body to produce increased amount of adrenaline, which causes increased blood pressure, heart rate; similarly carbon monoxide results in reduced oxygen flow rate in the blood stream. Smoking increases the levels of fibrinogen and platelet aggregation, which brings about the stickiness of the blood vessels and cells; it subsequently allows cholesterol to build as fatty deposition⁵¹. Long term smoking results in decreased levels of HDL, increased levels of LDL.

Diet and Hypertension

Unhealthy diet practices include high consumption of saturated salts, fats and low consumption of fruits and vegetables. This dietary imbalance provides a route map for the progression of cluster of complications into CVD. Various studies revealed the association of dietary fats and CHD. Diet and endogenous synthesis are the two sources for presence of Cholesterol in the blood and tissues. But the association of dietary cholesterol and CVD hypothesis is still proved to be contradictory⁵². However these dietary changes ultimately pave way into hypertension. Increased salt intake and hypertension directly increases further risks of CVD.

Non-Modifiable risk factors**Age and gender**

The prevalence of CVD rates increases with age. According to World Health Organization (WHO) age is considered as one of the powerful independent risk factor for CVD. Studies also

proved the appearance of fatty streaks in foetus stage itself. Even though CVD occurs in childhood, adulthood stage, but once age limits crosses 55, incidence rates double every decade. In terms of gender, men are more prone to CVD compared to women. Statistical data's also proves men (50%) and women (33%) develop CHD in their lifetime⁵³.

Genetics

Enormous studies are focused on risk factors like smoking, diet, physical activity etc., but in recent times focus is shifted towards role of genes in the onset of CVD. On account of this several data's suggesting CVD have linked with heredity. Studies also quoted polymorphisms and linkage markers are linked with CVD⁵⁴.

CONCLUSION

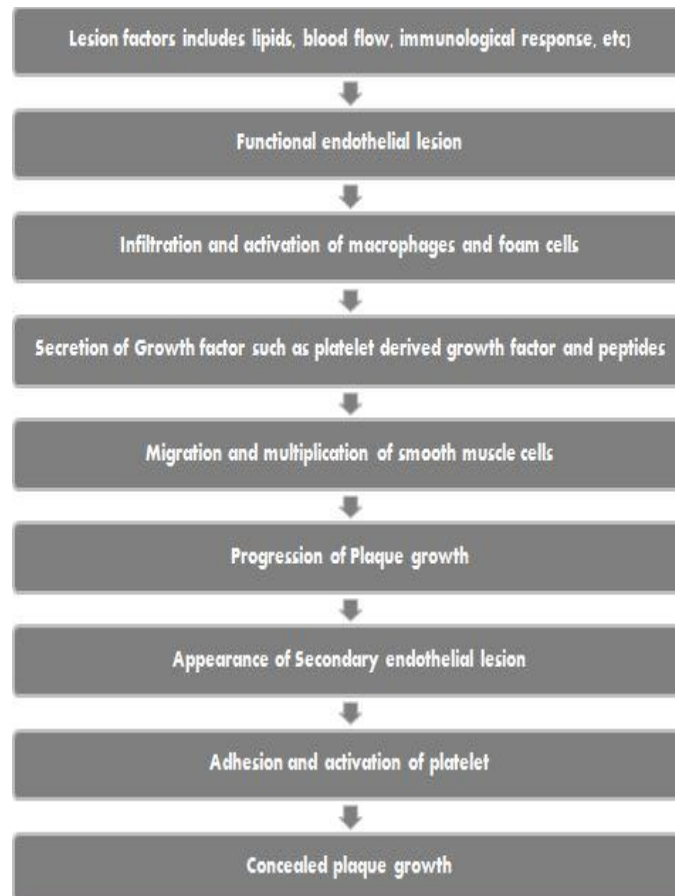
Once, when the universe was predominantly dominated by communicable diseases and malnutrition, mortality rate was out of control. As we walked off for the betterment of life, the trends in universe also started to shift in all means. Such shift brought an improvement in tackling poverty, famine & fatal infectious disease. But this transition resulted in the emergence of different forms of cardiovascular diseases. Majority of the risk factors are accompanied by our life style changes. From this review it is evident that CVD imposes a major threat for the life. It is necessary to monitor, the risk factors for atherosclerosis in foetus stage itself, as it sets a platform in the pregnancy period, to evolve into bigger threat in adult stage. Though public awareness regarding CVD is in practice, it still needs to reach to all corners of the population. Throughout the world, government sectors have already imposed restrictions in the usage of tobacco products and alcohol, but still mortality rates are at the peak level. This indicates still more restrictions and surveillance are needed to be carried out at the elementary level. Even though smoking and alcohol consumption are not the only factors for CVD, we need to focus on proper diet right from childhood stage. In future it's mandatory that several interventional programmes should be implemented at national level to eradicate these deadly diseases from our planet. Though several safety measures and awareness programs are in practice, yet proper healthy and dietary habits have to be followed in order to minimize the progression of CVD.

Table 1: Major CVD risk factors among countries

Risk factors	Countries
Hypertension	India, Japan, China, United States of America, West Indies).
Dietary methods	United Kingdom, United states of America
Smoking	India, Mexico, United states of America
Diabetes	India.

Table 2: Basic outline about Arteriosclerosis and Atherosclerosis

Arteriosclerosis	Atherosclerosis
Condition refers to hardening of arteries conveyed with loss of elasticity, which ultimately results in stiffness.	It is common type of arteriosclerosis and characterized by hardening of arteries.
It has three types <ol style="list-style-type: none"> 1. Atherosclerosis. 2. Arteriolosclerosis (thickening of walls of arterioles) 3. Monckeberg's Calcific Sclerosis or Medial Calcific Sclerosis (commonly occurs in uterus & thyroid, calcification of internal elastic lamina) 	Caused by plaque formation. Plaque generally composed of Lipids, cholesterol.

**Fig. 1: Events in Plaque formation****REFERENCES**

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