REVIEW ARTICLE

A Comprehensive View on Cardiovascular Diseases (CVDs): Genetics, Risk Factors & Preventions

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ABSTRACT

Cardiovascular Diseases (CVDs) are one of the foremost causes of deaths across the world. This review aims to evaluate the genetics and risk factors involved in CVDs and to assess the preventive measures which can be taken for diminishing the chances of developing CVDs. The goal of this review is to provide researchers and clinicians dealing with vascular disorders with a compendium of data about the genetic causes, risk factors, and preventive strategies to combat the development of CVDs. We searched online databases including PubMed for peer-reviewed scientific papers, case studies and review articles related to CVDs, emphasizing on the role of genetics and risk factors like diabetes, hypertension, smoking, alcohol consumption, obesity, age & gender in the progression of CVDs, and reviewing the role of diet and exercise in the prevention of CVDs. Managing the risk factors involved in CVDs is the most essential step for the inhibition of vascular diseases. Healthy lifestyle interventions consisting of a well-balanced diet and physical activity are very critical for the prevention of CVDs. Trials carried out on model organisms have indicated a direct link between diet and exercise on cardiovascular conditions. Strategies involved in the treatment of vascular diseases should also include low-fat diet plans like consumption of whole grains, fruits, vegetables, yogurts and avoiding high-saturated fat-containing foods with the addition of performing moderate aerobic exercises including cycling, swimming, hiking, and running to eliminate the root of the problem.

Keywords: Cardiovascular Diseases (CVDs), Genetics, Cardiovascular Risk Factors (CRFs), Preventive Measures, Diet & Exercise, Model Organ

INTRODUCTION

Cardiovascular diseases (CVDs) are termed as disorders of the heart and blood vessels. A number of these heart disorders are caused due to the lack of physical activity and inadequate diet. Some genetic factors also play a key role in developing numerous heart complications. CVDs have become the leading cause of premature deaths in countries across the globe. Many risk factors are involved in increasing the chances of evolving vascular disorders. Some of the major risk factors include (1) Diabetes, (2) Hypertension, (3) Smoking, (4) Alcohol Consumption, (5) Obesity, (6) and Age & Gender. CVDs can sometimes be classified based on their causing factors. Vascular disorders can be caused due to partial or complete blockage of blood vessels. For example, Thrombosis (Formation of the

clotted mass of blood within a vessel). Some of the widely occurring heart disorders include Atherosclerosis, Angina Pectoris, Myocardial Infarction (Heart attack), etc.

In addition to the commonly known CVDs, there is a different class of heart problems known as congenital heart diseases (CHDs), heart disorders that are produced in fetal life and occur as birth defects. The majority of these are caused due to genetic mutations. For example, patent ductus arteriosus (PDA), is a birth defect in which the ductus arteriosus fails to close after birth causing the mixing of oxygenated and deoxygenated blood. Infants with this disorder are referred to as Blue Babies.

Hypertension is caused due to high blood pressure. Factors that are a basis for high blood pressure also lead to many occurring CVDs. Various treatments are present for curing different CVDs. In the case of most of the heart disorders, surgeries are performed, and drugs are administered for treatment. Broadly used methods for surgical treatment include angioplasty, coronary bypass, and open-heart surgery.

The increase in CVDs in the past few years has been linked to an unhealthy lifestyle, physical inactivity, high cholesterol levels, and high blood pressure. The risk factors involved are directly contributing to causing CVDs. Genetics also plays a key role in susceptibility to major risk factors. As the treatments involved in curing CVDs are long, time-consuming, and costly processes, it would be easier to understand the risk factors involved and take appropriate measures for the prevention of heart diseases. Without taking in to account the causative factors, effective treatment cannot be developed for any disease. CVDs are one of the leading causes of deaths worldwide, so developing preventative measures against them is a major step forward towards saving countless lives.

Genetics: Influence on Cardiac conditions

Inherited cardiac conditions (ICC) are a sub-type of CVDs caused by genetic changes including SNPs, mutations, and epigenetic change (Care et al., 2017). A Variety of studies have indicated a link between CVDs and genetic conditions (Moser., 1985).

The diagnosis of heart disorders and stroke varies in people of different ethnic backgrounds. People belonging to Asian backgrounds are at twice the risk of developing CVDs as compared to their European counterparts (Aambo & Klemsdal., 2017; Martin., 2018). Genetic variations occurring genes involved in autoimmune pathways, can eventually lead to vascular disorders (Perrotti et al., 2017).

In the case of congenital heart diseases (CHDs), four different categories of genes have been identified which lead to abnormal heart conditions (Arcelli et al., 2010). About 400 genes are linked to causing CHDs (Jin et al., 2017). Approximately 35% of congenital heart diseases in patients are caused due to genetic factors (Simmons & Brueckner., 2017). Many of the existing CHDs occur in African nations like Rwanda, where genetic defects are very common (Teteli et al., 2014). Transcription factors and their enhancers are also involved in causing CHDs. Overexpression of transcription factors (*TBX5, NKX2-5,* and *GATA4*), and their enhancers (*MYH6 & NPPA*) has been shown to cause the defect in drosophila (Amodio et al., 2012).

Table 1 shows a list of Genes and their effects related to CHDs occurring in humans. Studying the effects of these genes affiliated with the occurrence of CHDs can help design novel therapies for the diagnosis and treatment of vascular disorders.

Table 1: Genes associated with the development of Congenital heart diseases (CHDs).

Genes	OMIM ID	Normal Function	Resulting Defects	References
SMAD3	603109	Intracellular signals transducer	Increase risk of ventricular septal defects (VSDs)	(Li et al., 2015b)
ACTA2, FBN1 TGFBR2	102620, 134797, 190182	Protein formation	Bicuspid aortic valve disease	(Giusti et al.,2017)
TBX20 CASZ1	606061, 609895	Transcriptional regulation	Dilated cardiomyopathy	(Kennedy et al., 2017)
LEFTY1 LEFTY2	603037, 601877	Left-right Asymmetry during development	Increase risk of CHDs	(Deng et al., 2014)
TCN2	613441	Transport proteins	Increase risk of CHDs	(Li et al., 2017)
MTHFR, MTRR	607093, 602568	Amino acid synthesis	Increases risk of VSDs	(Noori et al., 2017)
FOXC1	601090	Embryonic development	Multiple CHDs	(Du et al., 2016)
ALPK3	617608	Cellular differentiation	Primary cardiomyopathy	(Çağlayan et al., 2017)
ZW10	603954	Chromosomal segregation	Associated with CHDs	(Sun et al., 2018)
GATA4, JAG1, FOXC2, TBX5, TBX1	600576, 601920, 602402, 601620, 602054	Transcriptional factors and developmental regulation	Multiple CHDs including Conotruncal defects (CTDs)	(Morgenthau et al., 2018; Zhang et al., 2018)
MESP1	608689	Transcriptional proteins	Increases risk of VSDs	(Zhang et al.,2017)
MSX1 MSX2	142983, 123101	Transcriptional regulation	Associated with causing VSDs	(Li et al., 2015a)
NKX2-5	600584	Transcriptional factors	Impaired cardiomyogenesis	(Anderson et al., 2018)

Genetic mutations lead to complete heart failures (HF) in patients with ventricular disorders such as right ventricular apical (RVA) and atrioventricular block (AVB). Mutation in *LMNA* and *SCN5A* genes increases apoptotic rate, leading to the onset of early heart failure in (AVB) patients (Liu et al., 2017).

Coronary artery diseases (CADs) are among the most widely spread heart-related disorders. They are influenced by environmental as well as genetic components. Studies have shown a relation between *MPO* gene and CADs. Therefore, people with single nucleotide polymorphisms in *MPO* gene are at significantly greater risk of developing CADs. Similarly, individuals with *IL-1beta* allele are more prone, towards CADs (Sreekanth et al., 2016; Arslan et al., 2017). Point mutations in *ADD1* and *ACE* genes have been observed in causing arterial hypertension (Cieslewicz & Jablecka., 2010).

Apolipoprotein E (Apo E) is involved in maintaining cholesterol levels. Decreased activity of the transcription factor phosphatase 1G reduces ApoE levels, which leads to several vascular disorders (Benson et al., 2017).

NO-cGMP Pathway Regulation

The Nitric oxide-cyclic guanosine monophosphate (NO-cGMP) pathway (Figure 1) plays an imperative role in maintaining blood pressure, normal cardiac function, and cardiovascular homeostasis in the human body.

Nitric oxide (NO) is produced by endothelial nitric oxide synthase (eNOS) in the vascular endothelial cells of the arteries. NO eases blood flow and regulates vascular function by promoting vasodilation of blood vessels (Grassi et al., 2013). When increased blood flow is detected by the receptors due to any exogenous signal, nitric oxide is produced by eNOS in the endothelial cells which is then transferred to the nearby smooth muscle cells, in which NO acts as an intracellular signal. NO contributes towards the enzyme guanylyl cyclase as it converts GTP to cyclic GMP, resulting in smooth muscle relaxation and thus, contributing toward lowering the blood pressure. NO also protects the veracity of the endothelium and regulates vascular homeostasis by inhibiting leuko - cyte adhesion, proliferation, vascu- lar inflammation, platelet adhesion, and aggregation of vascular smooth muscle cells (Forstermann & Sessa., 2012).

The NO-cGMP pathway is regulated by several genes (Table 2). Single nucleotide polymorphisms (SNPs) in corresponding genes like *ARG1*, *NOS3*, *GUCY1A3* and *PRKG1* results in NO deficiency by reducing eNOS activity, this eventually leads to the occurrence of numerous CVDs (Leineweber et al., 2017).

Cardiovascular Risk Factors (CRFs)

Diabetes

The coronary risk associated with diabetes increases the chances of developing coronary heart disorders (Davis et al., 2014). Type 2 diabetes mellitus (T2DM) is linked with many vascular disorders including coronary artery diseases (CADs), congestive heart failure (CHF), and myocardial infarction (MI). Due to genetic factors, poor glycemic control, and metabolic degradation, the chances of complete heart block (CHB) increases in diabetes patients

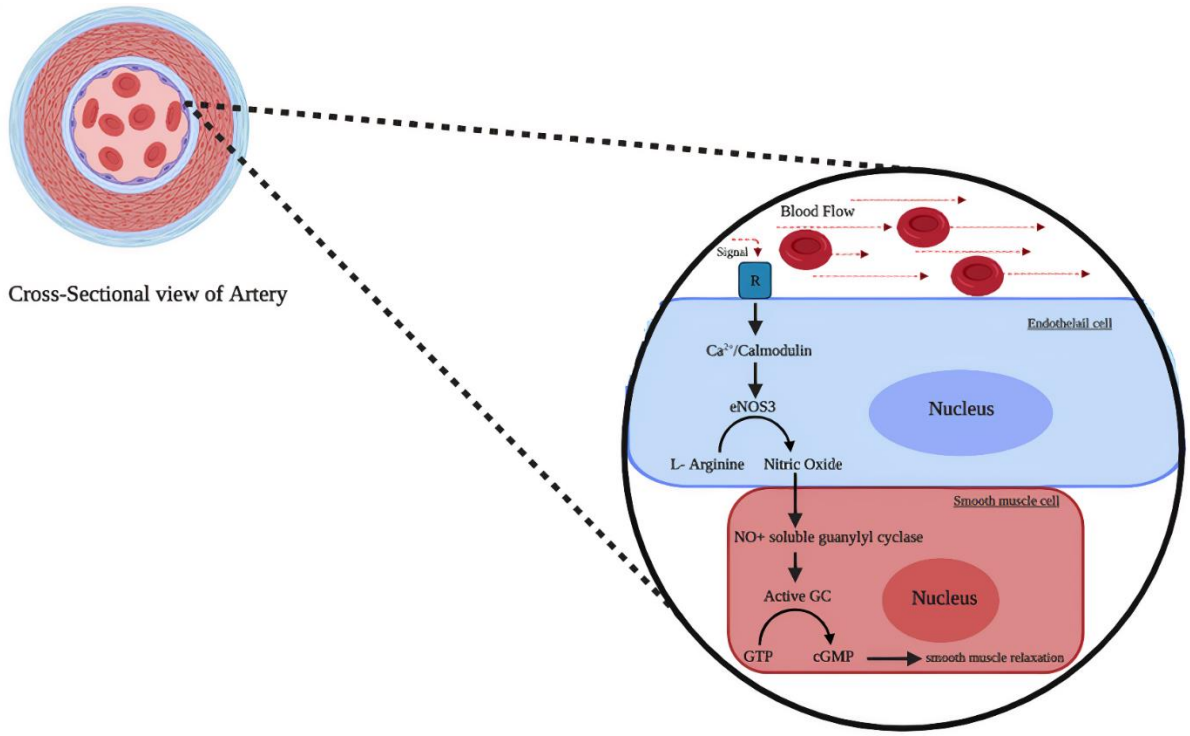

Figure 1: NO-cGMP Pathway: eNOS= endothelial nitric oxide synthase; R= receptor; NO= nitric oxide; GC= guanylyl cyclase; GTP= guanosine triphosphate; cGMP= guanosine monophosphate

(Agarwal & Singh., 2017; Martin., 2017a). The mortality rate increases in type 1 and type 2 diabetic patients with atherosclerosis caused due to the development of CVDs. A strong link between insulin resistance and atherosclerosis has been observed which is caused by ineffective insulin receptor (IR) signaling. Using inhibitors like (Trodusquemine) to reduce the activity of protein tyrosine phosphatase 1B (TP1B), which is a major regulator of IR, has shown prevention of plaque formation and reversal of atherosclerosis (Thompson et al., 2017). Whole-body glucose uptake as a response to insulin is termed as meal-induced insulin sensitization (MIIS). Insulin induces the release of hepatic insulin sensitizing substance (HISS) causing uptake of glucose in kidneys, heart, and skeletal muscles. Impairment of (HISS) release, occurs due to the absence of MIIS causing hyperglycemia and hyperinsulinemia which leads to vascular dysfunction and cardiac problems (Chowdhury et al., 2013).

Diabetes has also been observed to be caused by postprandial blood glucose concentration in middle-aged women (45-50 years). moderate level of a walk after a meal can help decrease blood glucose level (Nygaard et al., 2009).

Although CVDs are correlated with diabetes and vice versa, the risk of developing type 2 diabetes in patients suffering from cardiac abnormalities is 2-4 times higher than in the general population (Kristjansson et al., 2015). Type 2 diabetes

can be prevented by up to 28-59% by lifestyle changes like performing physical activities taking a low-fat diet and reducing mental and physiological stress (Walker et al., 2010; Martin., 2017b).

Red cell distribution width (RCDW) serves as a marker for detecting CVDs in patients with diabetes (Al-Kindi et al., 2017). Identifying diabetes in patients is the first step towards treatment, some amino acids like isoleucine, phenylalanine, and tyrosine show metabolic signatures which can help predict diabetes development in patients. Studies indicate aromatic and branched-chain amino acids as efficient markers for detecting susceptibility to CVDs in diabetic patients (Magnusson et al., 2013).

Table 2: Genes involved in the NO-cGMP Pathway

Gene	OMIM ID	Normal Function	Resulting Defects	References
ARG1	608313	Urea Cycle/ Arginine synthesis	Myocardial Infarction	(Mónica et al., 2016)
ARG2	107830	Urea Cycle/ Arginine synthesis	Myocardial Infarction	(Zhang et al., 2019)
GCH1	600225	GTP cyclohydrolase I Synthesis	Hypertension	(Guo et al., 2017)
NOS3	163729	Nitric oxide synthesis	Myocardial Infarction,	(Bogdan, 2015)
DDAH1	604743	Methylarginine levels / Inhibits NOS	Hypertension	(Xu et al., 2017)
DDAH2	604744	Methylarginine levels/ Inhibits NOS	Hypertension	(Klinger & Kadowitz, 2017)
GUCY1A2	601244	GTP conversion	Hypertension, Coronary artery disease	(Wobst et al., 2018)
GUCY1A3	139396	NO receptor	Coronary artery disease	(Kessler et al., 2019)
PRKG1	176894	Smooth muscle relaxation	Hypertension	(Han et al., 2019)
PDE5A	603310	Hydrolysis of cyclic nucleotides	Hypertension	(Ueda et al., 2019)
NPPA	108780	Cardiac homeostasis	Heart failure, Hypertension	(Menon et al., 2019)
NPR3	108962	Vascular homeostasis, Fluid balance	Hypertension	(Gao, 2017)

HYPERTENSION

Anxiety, depression, and mental trauma lead to stress. Individuals belonging to different ages, ethnic backgrounds, and genders are affected differently by stress. Genetic variations caused by stress can lead to CVDs (Albert et al., 2017). Salt intake is important

for preventing hypertension and vascular diseases (Ando et al., 2013)

In the U.S, the increase in mortality rates due to heart failure, stroke, and coronary artery diseases are higher in the African American population than in the White population, because African Americans are more prevalent towards hypertension due to greater stress (Carnethon et al., 2017).

Major depression disorders (MDDs) are linked to patients suffering from coronary heart diseases. Depression and vascular disorders including many risk factors have led to the 'Vascular Depression' Hypothesis (Iosifescu et al., 2005).

Depression disorders are associated with an increased level of tumor necrotic factor-alpha and interleukin-6. It has been observed that higher levels of C-reactive proteins (CRP) are present in patients with MDDs, and elevated CRP levels are inter-related with CVDs. Genetic factors may also influence CRP levels (Kozlowski et al., 2006).

Post-traumatic stress disorder (PTSD) is often shown in CVD patients. Increased cytokines and homocysteine levels usually occur in (PTSD) (Brown et al., 2009; Goldstein et al., 2015; Sagud et al., 2017; Sawchuk et al., 2005). About 34% of adults in the U.S suffer from hypertension (Kones & Rumana., 2014). The major cause of death in pregnant women in the U.S is due to CVDs caused by physiological stress. About 33% of death in the U.S occur due to vascular disorders (Graves & Davis., 2018).

Smoking

Majorly occurring disorders including cancers are associated with smoking. The risk of liver, lungs, and colorectal cancer increases with smoking. An estimated 85% of lung cancer occurs in smokers (Sealock & Sharma., 2018). Many CVDs are linked to smoking. Irregular patterns of cardiac rhythms are often observed in smokers. Although smoking affects every individual differently, people who suffer from bipolar disorder (BP-1), schizophrenia and severe mental disorder (SMD) are more prone towards the development of hypertension and vascular disorder due to smoking (Birkenaes et al., 2007; Foguet Boreu et al., 2013; Goldstein et al., 2009).

Young adults (aged 18 to 30 years) and people belonging to South Asian ethnicity are at higher risk of developing early Atherosclerotic Cardiovascular diseases (ASCVD) due to many risk factors including smoking (Gooding et al., 2017; Kandula et al., 2015; Jelwan et al., 2020).

Smoking eventually leads to cancer, high blood pressure, vasoconstriction, coronary heart diseases, and organ damage. Patients with chronic kidney diseases (CKDs) are 10 times more likely to die of vascular disorders correlated to risk factors like smoking (Gregg & Hedayati., 2018). Although many individuals do know about the detrimental effects of smoking, very few take appropriate steps to quit smoking. A study carried out on patients with CVDs to investigate that if they were aware of the risk factors involved with vascular disorders indicated that 30% of the patients identified smoking as a leading risk factor (Montinaro et al., 2008).

Alcohol

Alcohol consumption has toxic effects on the heart and vascular system. It has multiple synergistic and synchronous consequences

on the human body. Excessive alcohol intake causes dilated cardiomyopathy, induces arrhythmias, decrease myocardial contractibility, which leads to cardiovascular dysfunction, and causes tissue damage. Prolonged consumption of alcohol increases the risk of HF, hypertension, and CADs (Fernandez-Sola., 2015). Coronary atherosclerosis is often seen in patients with alcoholic cirrhosis (Danielsen et al., 2018).

Atrial fibrillation (AF), one of the most widely occurring forms of cardiac arrhythmias is interlinked with alcohol consumption and some other risk factors (Naser et al., 2017). The chances of developing CVDs increase with the increased ingestion of alcohol from light, moderate to heavy intake (Goel et al., 2018). Excessive alcohol consumption (>14 units/week) increases the risk of mortality (Luksiene et al., 2017; Saito et al., 2018).

Alcohol consumption is among the three leading causes of premature deaths in the U.S, just behind smoking, and obesity. The risk of premature deaths is higher in males aged (15-49 years) due to alcohol abuse than it is in females of the same age group (O'Keefe et al., 2018; Flora & Nayak., 2019).

Different types of alcoholic beverages have different effects on the vascular system, increasing the risk of CVDs.

Obesity

The increase in chronic heart diseases around the world is directly related to the rise in obesity rates in developing countries, especially in U.S. About one-fifth of the children in the U.S and two-third of the adults in the U.S are overweight or obese. Recent studies have shown that 33% of the U.S population is obese (Allison., 2017; Khan et al., 2009). The risk of developing CVDs rises in overweight individuals (BMI >/=25kg/m2) or higher, than in individuals with normal body weight (Eguchi et al., 2014). Although excessive eating is associated with obesity, some genetic factors that also influence a person's (BMI) (Goodarzi., 2018).

Obesity is a major lifestyle-based health complication (Lappalainen et al., 2014). Self-care is required for the prevention of obesity, which includes maintaining ideal body weight, and taking an adequate amount of nutrients (Frohlich & Al-Sarraf., 2013; Riegel et al., 2017). CVDs caused by obesity are one of the major causes of unnatural death among the population (Slockers et al., 2018).

Age and Gender

The risk factors intricated with vascular disorders have different effects on males and females belonging to different ages. The mortality rate due to ST-elevated myocardial infarction (STEMI) is twice in elderly females (>=65 years) than it is in elderly males (Juhan et al., 2018). Similarly, the effect of stress is higher on the elderly population as compared to the younger generations (O'Neil et al., 2018; Martin., 2016). The susceptibility to high blood pressure, hypertension, diabetes mellitus, and CVDs is also greater in aged individuals.

Prevention strategies against CVDs

Role of Diet

While considering the preventative measures which can be taken against CVDs, it is very

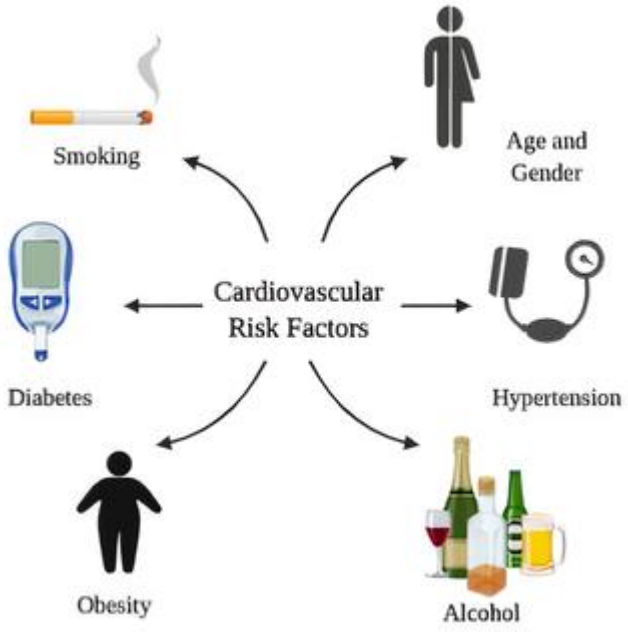

Figure 2: Systematics representation of risk factors involved in cardiovascular disorders

essential to address the root of the problem. An appropriate diet is the first step involved in the prevention process (Franklin et al., 2014). For the promotion of cardiovascular health, diet is vital to maintaining a healthy lifestyle by reducing the intake of saturated fats and increasing consumption of fresh fruits and vegetables (Anderson., 2018; Pouya et al., 2017).

It has been observed that foods that are rich in high anti-oxidants, like fresh fruits and vegetables, help reduce the risk of developing CVDs (van der Bom et al., 2002). Diet is considered the most significant factor while addressing the risks involved in CVDs. An adequate diet is associated with maintaining normal blood pressure and preventing ischemic heart diseases (IHD) (Arentoft et al., 2018). Taking the proper diet and adopting a healthy lifestyle greatly reduces the risk of Atherosclerotic cardiovascular diseases (ASCVD) in adults (Booth et al., 2016).

Excessive intake of high-fat containing foods leads to obesity, which results in hypertriglyceridemia, high blood pressure, and elevated cholesterol level. Ingestion of foods that are low in unsaturated fats can help prevent many coronary heart diseases (CHDs). Reducing the level of lipoprotein in the body also reduces the risk of developing CHDs. Patients with hypercholesterolemia, hypertension and diabetes mellitus are at greater risk towards the development of CHDs due to penurious eating habits. After the age of 40, the chances of developing CHDs in such patients increases 25% every 10 years.

A diet containing a moderate level of low-density lipoprotein (LDL) and decreased level of cholesterol can help prevent

hypercholesterolemia (Simoons & Casparie., 1998). Refined sugar, starch, and carbohydrates in western diet have fatalistic effect on health and increase the risk of CHDs, while unsaturated fats have beneficial impacts on metabolic health and reduce the risk of CHDs (Willett., 2008).

Consumption of dairy products such as cheese and yogurt having anti-inflammatory properties, high nutritional value. and low-fat content can help prevent vascular diseases and have a positive effect on health (Lordan et al., 2018).

The risk of developing age-related CVDs greatly increases with a decrease in leukocyte telomere length (LTL). It serves as a marker for detecting cellular aging. Studies have indicated a link between consumption of processed red meat with shortening of LTL thus, contributing towards the early onset of development of age-related diseases (Fretts et al., 2016).

Foods like whole grains, fish oils, beans, walnuts, and almonds are also crucial for healthy vascular system. Flavonoids present in cocoa and dark chocolates have efficacious effects on cardiovascular health and display a cardioprotective role. Chocolate intake (1-5+ times/week) has shown to reduce the risks of developing CHDs (Djousse et al., 2011). Flavonoids intake in the form of fruits and vegetables reduces the risk of CVDs (Jacques et al., 2015; Wang et al., 2014).

Role of Exercise

Reducing body mass is an essential step involved in the preventative process. The risk associated with developing vascular disorders rises with obesity. Physical activity programs are recommended along with healthy diet plans to decrease obesity and lower the risk of developing CVDs (Pate et al., 2015).

The risk of coronary heart diseases (CHDs) increases with physical inactivity. Exercise helps maintain a normal blood glucose level and has positive impacts on cardiovascular conditions. Daily exercise can prevent several health-related issues (Opie & Dalby., 2014). Although the risk of developing CHDs varies from person to person, the effect of physical inactivity combined with poor diet and other risk factors are more prominent in peoples belonging to South Asian backgrounds (Arjunan et al., 2013; Fernandez et al., 2014). Moderate exercises like (jogging) improve endothelial functions in arteries, protecting vascular systems from the detrimental effects of a high-fat diet (Bond et al., 2015).

Studies have shown that aerobic and resistance exercises (like running, swimming, and hiking) can reduce abdominal obesity in women, reducing the risk of atherosclerosis (Choo et al., 2014). Cycling, walking, sports, and other physical activities can help reduce the risk of CHDs in older individuals (Koolhaas et al., 2016). Self-care and self-management through exercises are important for the prevention of heart failure (HF) (Lee et al., 2009). Physical activities, lifestyle modifications, and good nutrition can help prevent many CVDs. Taking a low-fat diet combined with aerobic exercises reduces BMI, decreases LDL levels and increases HDL levels, which also lowers the risk of developing atherosclerotic cardiovascular diseases (ASCVD) (Cugnetto et al., 2008; Wenger., 2014).

Training exercises and physical activities can help in weight loss (~2kg), preventing

obesity and improving health (Swift et al., 2014). Continuous physical activities and aerobic exercises like cycling, hiking, swimming, and running are recommended for cardiac rehabilitation patients as they increase ventricular function and improve vascular health (Bjarnason-Wehrens et al., 2004; de Gregorio., 2018).

Some epigenetic changes like DNA methylation can be caused by performing physical activities, which play a vital role in the prevention of CVDs (Recchioni et al., 2017). The effects of exercise on an individual to reduce the risk of developing CVDs have been studied in numerous trials. Results show that (55-65 minutes) exercise performed at the rate of 4-5 times a week significantly reduces heart rate, lowers BMI and decrease HDL and LDL levels thus, enhancing performance levels of individuals as compared to (45-55 minutes) exercise performed at the rate of 2-3 times a week (Noe et al., 2014).

Trials on Model Organisms

Obesity has been linked to several vascular disorders in humans, mainly due to a diet consisting of high-fat content and a lack of physical activities. The chances of developing CVDs increase significantly with physical inactivity combined with a diet consisting mostly of high saturated fats. Preventative measures like exercise and low-fat containing diet, which reduces the risk factors influencing our cardiac health have been studied in model organisms.

Tests carried out on mouse models have shown a clear link between exercise and effects of a high-fat diet on cardiac conditions in Table 3, which can help in designing effective treatments against CVDs. Trials carried out on model organisms can help provide data for attaining new drug therapies, which in turn can lead to the treatment of various vascular disorders.

Model organisms are being used for functional studies of arterial systems. In vivo experiments using optical coherence tomography (OCT) have been utilized for analysis of the vascular function of arteries in mouse models. The OCT method allows for determining flow resistance and inner diameter changes in the arteries of model organisms. Techniques like OCT can help us in detecting early-stage vascular dysfunction in mouse strain. thus, providing a better understanding of the disease mechanism (Muller et al., 2017).

CONCLUSION AND FUTURE PROSPECTS

Looking forward to the future of drug development and strategies for contending against the increased rate of CVDs, it has become relatively clear that newly developed treatment might not only be as economically sufficient for every individual suffering from a vascular disorder. The goal for health care providers and researchers should be to develop low-fat containing diet plans, in addition to physical training programs for patients suffering from CVDs.

Public health measures against CVDs involve costly medication, which also has adverse side effects on individual health. The increased cost and side effects of modern medication have raised widespread concerns regarding the treatment strategies not only in developing countries but also in developed countries as well. The best way to combats CVDs is to employ preventive measures

Table 3: Consequence of High fat diet (HFD) and Exercise on various mouse model.

Experiments	Results	References
Active Mouse; **(fed with HFD; 16 weeks/ provided exercise on running wheel)** Inactive Mouse; **(fed with HFD; 16 weeks/ provided NO exercise)**	In the case of the active mouse; exercise prevented diastolic dysfunction; HO-1 protein level increased. In the case of the inactive mouse; Increased cardiac stress is observed with an increased risk of diastolic dysfunction.	(Bostick et al., 2017)
Experimental Mice; **(fed with HFD; 20 weeks/ provided moderate and high-intensity exercise training)** Controlled Mice; **(fed with HFD; 20 weeks/ NO exercise provided)**	In experimental mice; Exercise prevented cardiac dysfunction; Increased aerobic activity and decreased insulin resistance. In controlled mice; No change in aerobic activity; No decrease in obesity.	(Boardman et al., 2017)
Obese Mice Group; **(fed with HFD; Provided training exercise)** Obese Mice Group; **(fed with HFD; NO training exercise provided)**	Exercise decreases intramuscular triglyceride levels by activating lipolysis factors; thus, playing an important role in lowering obesity in the active mice as compared to in the Inactive mice.	(Ko et al., 2018)
Obese Mice (Group A); **(fed with high fat and sugar water diet; Provided high-intensity exercises with intermediate fasting)** Obese Mice (Group B); **(fed with high fat and sugar water diet; NO intervention)**	Exercise with intermediate fasting helps lower weight gain, lowers LDL levels and prevents fat accumulation in mice group provided with exercise as compared to in mice group with no intervention despite taking High-fat diet.	(Wilson et al., 2018)
Trained Obese Mice; **(fed with HFD; 16 weeks/ provided physical activity)** Untrained Obese Mice; **(fed with HFD;16 weeks/ NO physical activity provided)**	Decreased level of CLK2 protein prevented fat accumulation in the liver of obese mice provided with exercise as compared to in the untrained mice group.	(Muñoz et al., 2018)

before the health outcome emerges and become injurious to a person's health. Although there has been an increase in the rate of CVDs across the world, combining

medicine and preventative measures with a healthy lifestyle can help reduce the risk of developing CVDs. it is a common public expression that "prevention is better than cure". Combining physical activities with the consumption of low-fat containing a nutritional diet is the first step towards managing risk factors and preventing CVDs**.**

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COMPLIANCE WITH ETHICAL STANDARDS

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