



## A Study of Recent Cardio-Biomarkers in Myocardial Infarction : Atherosclerosis

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### ABSTRACT

Recent research review study highlights of Cardio-biomarkers in Myocardial disease especially atherosclerosis risk prediction advanced biomarkers by incorporating both traditional risk factors to be used as diagnostic markers and recent technologically generated diagnostic and therapeutic markers. This paper explains traditional biomarkers such as lipid profile, glucose, and hormone level and physiological biomarkers based on measurement of levels of important biomolecules such as Serum ferritin, triglyceride to HDLp (high density lipoproteins) ratio, Lipophorin-cholesterol ratio, Lipid-lipophorin ratio, LDL cholesterol level, HDLp and Apolipoprotein levels, lipophorins and LTPs ratio, Sphingolipids, Omega-3 Index, and ST2 level. In addition, immunohistochemical, oxidative stress, inflammatory, anatomical, imaging, genetic, and therapeutic biomarkers have been explained in detail with their investigational specifications. Many of these biomarkers, alone or in combination, can play important role in prediction of risks, its types, and status of morbidity. As emerging risks are found to be affiliated with minor and micro level factors and its diagnosis at an earlier stage could find coronary heart diseases, hence, there is an urgent need of new more authentic, appropriate, and reliable diagnostic and therapeutic markers to confirm disease well in time to start the clinical aid to the patients. Present Study aims to discuss new emerging biomarkers that could facilitate more authentic and fast diagnosis of Atherosclerosis especially Myocardial Infarction and disorders in the future Conclusively this huge target could not be achieved without making integrating efforts made by biochemists, immunologists, molecular biologists to unfold the mystery of CHDs, its more accurate diagnosis, and therapeutics as well.

### KEYWORDS

ASCVD: Atherosclerotic cardiovascular disease, GGT: Glutamyl transferase activity, PUFAs: Polyunsaturated fatty acids, MI: Myocardial Infarction, NAFLD : Nonalcoholic fatty liver disease

### INTRODUCTION

Atherosclerosis are increasing day by day due to over utilization of fats or due to genetic reasons. It is a leading cause of morbidity and mortality from infancy to old age. Though conventional risk prediction algorithms are made available on presence of major myocardial infarct risk factors identified in diseased population, authentic and accurate biomarkers of Coronary heart diseases are lacking. It not only delayed clinical diagnosis but also increased risk manifold and resulted in accidental death of patients. Therefore, an early identification and treatment of risk factors are much needed to accelerate disease prevention and morbidity improvement[1]. Numerous risk scores have been developed to predict myocardial risk. These scores are based on observations of the relative degree of importance of individual major risk factors. Till the date numerous physiological biomarkers based on serum lipid, glucose and hormone biomarkers serum lipid, glucose and hormone profile have been identified that are associated with increased cardiovascular risks. Some of them are simple traditional biomarkers based on lipid profile and risk factors. More often, levels of plasma, serum, and blood are proved to be best risk biomarkers [2]. These markers display cellular lipid interactions and physiological functions of serum lipid bearing proteins and assist in clinical decision making and authenticated risk type [3]. There are so many established cardiovascular risk markers based on confirmed clinical outcomes related to biomolecules, its structure, and functions. There are new mini- and microlevel clinical factors associated with an elevated prospective risk of developing coronary heart diseases.

However, to establish risk status measurement of a standard lipid profile, including total cholesterol, LDL (low-density lipoprotein) cholesterol, HDL (high-density lipoproteins) cholesterol, and triglycerides, is recommended from an integral component of approaches to cardiovascular risk prediction. These old markers, such as elevated LDL cholesterol, hypertension, diabetes, and low LDL cholesterol, smoking, and family history can predict premature coronary heart diseases in man. Most important prediction is made by Framingham 10-year risk score which is commonly used to predict cardiovascular event over the next ten years in the primary prevention of disease. Hence, a need persists for diagnosis of CVDs at two stages: first category of patients stratified as low risk (Framingham 10-year risk score >10%) requires less risk identification, modification, and treatment method, but patients stratified as high risk (Framingham 10-year risk score >20%) need intensive risk factor identification. For more appropriate judgment of CHDs, this score incorporates age, total cholesterol, HDL cholesterol, smoking status, systolic blood pressure, and gender [4]. On the basis of scores obtained in patients, these are classified in three groups as scores of <10% low, intermediate 10–20%, and high >20% risk (Table 1). Last category of patients is confirmed as atherosclerotic disease patients and needs early intensive clinical care and factor modification [4] (Figure 1). More specifically, patients with a 10-year risk >20% or with diabetes are considered to be coronary heart disease risk equivalents in terms of the approach to risk modification [5] (Table 1).

**Table 1: Important emerging risk biomarkers in cardiovascular disease and disorders.**

Name of disease	Effects	Risk score	Biomarker	References
Homozygous familial hypercholesterolemia	Premature cardiovascular morbidity and mortality	10–20%	Total cholesterol, LDL cholesterol	
Hypertriglyceridemia/hypertriglyceridemia	Elevated levels of Lp(a)	20%	Lipid profile	
Chronic kidney disease	Elevated levels of Lp(a)	10%	Lipid profile	
Cholelithiasis	Gall stone formation due to cholesterol and salts	20%	LDL cholesterol and small dense LDL particles	

Homozygous familial hypercholesterolemia	Premature cardiovascular morbidity and mortality	10–20%	Total cholesterol, LDL cholesterol	
Atherosclerosis	Arterial obstruction, chest pain	20–25% ABCA1 efflux	Polyunsaturated fat (PUFA) and carbohydrates, serum -glutamyl transferase activity, blood genomic profiling, and 47 integrin (LPAM-1)	[6, 7,45–48]
Coronary heart disease	Monocytosis, high diabetics, hypertension, and chronic kidney diseases	20%,	Impaired sterol efflux, efflux capacity of high-density lipoprotein, HDL), myeloperoxidase increasing circulating HDL	[7]
Hyperglycaemia or type 1 diabetes	CVD and mortality	25%,	(TC), (TG), HDL, LDL, and anthropometric and biochemical parameters	[8]
Dyslipidemia	Hypoperfusion, high inflammation, and low BP	10%	TC, (TG), HDL, LDL, and anthropometric and biochemical parameters	[8, 42]
Atherosclerotic peripheral arterial disease	Prevalent, morbid, and mortal diseases	20% Shortening of lumen	LDL cholesterol	[9]
Ischemic heart disease (IHD)	Endothelial dysfunction, vascular inflammation	10–20%	Lipids, cholesterol, calcium, and cellular debris	[11]
Diastolic dysfunction and diastolic heart failure	Asymptomatic hypertension	20%	Myocardial remodeling	[12]
Chronic heart failures	ADP-induced platelet aggregation, triglycerides, end-diastolic volume, end-diastolic dimension, and ventricular septal thickness death	15–20%	Lipidemic, hemostasiological, and hemodynamic indicators, Willebrand factor, and D-dimer,	[13]
Myocardial infarction	Very high morbidity, severe pain	20–25%	Circulating microRNAs level in patients	[17]
Lipid stress and storage	Influence cholesterol availability in lipid rafts in immune cells	High LDL/HDL cholesterol levels	Omega-3 Index	[15, 16, 18]
Neuronal dysfunction	Neuronal cell death and neuroinflammatory	10–15%	27-hydroxycholesterol, plasma HDL, N-acyl ethanolamines (NAEs)	[21]
Transient global cerebral ischemia	Cardiac arrest and cardiovascular problems	5–10%	-3 PUFAs	[22]
Hypoglycaemia	Cardiac implications	5–10%	Elevated levels of Lp(a) and low HDL cholesterol	[23]
Hypertriglyceridemia/coronary artery disease (CAD)/acute coronary syndrome	Severe effect on BMR and peripheral and cardiac circulation	5–10%	Altered serum lipid	[1, 33]
HDL metabolism disorders	Severe inflammation and pain	5–10%	Lipid droplets (LDs)	[24]
Nephrotic syndrome	Renal filtration checked	5–10%	LDL cholesterol, triglycerides, and Lp(a)	
Fatal myocardial infarction and brain stroke	Cardiovascular risks, morbidity, and mortality in elderly men	20–25%	Fat-specific protein Fsp27, fat storage-inducing transmembrane (FIT) proteins, seipin, and ADP-ribosylation factor 1-coat protein complex I	[24]
Systemic lupus erythematosus	Problem of PCV and hemoglobin	5%	Factors, proteins, ions, and stimulators of heart muscles	[34]
Acute myocardial infarction	Death of part of myocardial muscles, central chest pain, and severe crushing	20–25%	Serum soluble ST2 and interleukin-33	[36, 37]
Hypertension and dyslipidemia, hypercholesterolemia	Cardiovascular risk factors	15–20%	Total cholesterol and low-density lipoproteins	[41]
SCVRs	Tachyarrhythmias, bradyarrhythmias	5–10%	BP and LDL-C, high BMI	[43]
Hyperhomocysteinemia	High TC and pathogenesis	5%	LDL-C, HDL-C, TG, ApoA1, and ApoB Lp(a)	[44]
AVDs, type 2 diabetes, or metabolic syndrome	Increased levels of triglycerides, low levels of high density lipoprotein cholesterol, and postprandial lipemia	20–25%	MetS	[49, 50]
Procardiovascular risks, cardiovascular risks	Inflammation, obesity, and thrombosis	5–10%	Sedentary behavior, -trace protein from GFR marker	[38, 40, 51]
Metabolic lipid disorders	Circulatory dysfunctions, high BP, peripheral pain, and high or low BMR	5–10%	MALDI-MS, imaging and lipidomics for clinical diagnosis, and proteome analysis	[52, 53]
Ischemic heart disease	Circulatory dysfunctions	Smoking, hypertension, age, family history	Endothelial dysfunction, monocyte accumulation, endothelial apoptosis, and thrombus formation	[54]

Low HDL-C syndromes	Increased risk of CAD	5%	Sphingomyelin phosphodiesterase 1 and glucocerebrosidase	[55]
Hypothyroidism and gall stone	Severe pain, inflammation	5%	TSH level and sodium and potassium salts	[56]
Multiple CVDs, diabetes, stroke, and recurrent ischaemia syndrome	Hepatic inflammation due to common carotid intima-media thickness	10–20%	Multiple biomarkers, vascular imaging	[57, 58]
Angina pectoris	Obesity, arterial thickness, BMI and respiration rate, and severe chest pain	10–20%	Coronary angiography	[24]
Antiphospholipid syndrome	Venous thrombosis	5%	microRNAs	[59, 60]
Myocardial infarction	Pregnancy associated plasma protein-A (PAPP-A in serum)	15%	Severe blood pressure changes, central chest pain, and silent or knocking angina	[61]

Homozygous familial hypercholesterolemia (HoFH) is associated with severe hypercholesterolemia and premature cardiovascular morbidity and mortality. More often, increased cardiovascular risk has also been associated with the presence of obesity, hypertriglyceridemia, chronic kidney disease, and elevated levels of Lp(a) (Table 1). Moreover, level of saturated fat is inversely associated with atherosclerosis progression in post-menopausal women, whereas polyunsaturated fat (PUFA) and carbohydrates were positively associated [6].

Coronary heart disease is also associated with monocytosis, high diabetics, hypertension, and chronic kidney diseases. The efflux capacity of high-density lipoprotein (HDL) with cultured macrophages associates strongly and negatively with coronary artery disease status, indicating that impaired sterol efflux capacity might be a marker and perhaps mediator of atherosclerotic burden [7] (Table 1). More often, myeloperoxidase may contribute to the generation of dysfunctional HDL with impaired ABCA1 efflux capacity in humans with atherosclerosis. Quantification of chlorotyrosine and oxidized methionine in circulating HDL might be useful indicators of the risk of cardiovascular disease that are independent of HDL cholesterol [7] (Table 1).

More often, hyperglycaemia or type 1 diabetes plays a major role in increased incidence of CVD and mortality in individuals. Patients facing type 1 diabetes showed increase of premature mortality, primarily from cardiovascular disease (CVD) [8]. It also indicates that severe lipid disorders may occur in patients with type 1 diabetes, but the occurrence of elevated high-density lipoprotein cholesterol is positively associated with longevity of these patients (Figures 1). Similarly, nonrenal hypertension by itself is a significant risk factor for CVD but if adequately treated does not appear to mitigate against longevity [8]. In old ages (55–60) measurement of blood pressure and anthropometric and biochemical parameters such as total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), and low density lipoprotein (LDL) assist in finding high risk of CVD, dyslipidemia, and metabolic disorders in patients [8] (Table 1).

Atherosclerosis is the main cause of death in the world through causing ischemic heart disease (IHD) (Figures 1) It is peripheral arterial disease (PAD), most prevalent, morbid, and mortal disease [9]. It is one of the most common disorders among the elderly, because of depression prevailed in the old age and rates of very high atherosclerosis [10]. Atherosclerosis is characterized by endothelial dysfunction, vascular inflammation, and the buildup of lipids, cholesterol, calcium, and cellular debris within the intima of the walls of large and medium size arteries [11]. Therefore, new emerging biomarkers of myocardial remodeling can develop to identify asymptomatic hypertensive patients at risk for diastolic dysfunction and diastolic heart failure [12]. In addition, lipidemic, hemostasiological, and hemodynamic indicators associated with the risk of cardiovascular death in high- and very high-risk patients. The high levels of von Willebrand factor, D-dimer, ADP-induced platelet aggregation, triglycerides, end-diastolic volume, end-diastolic dimension, and ventricular septal thickness are independent predictors of cardiovascular death in very high-risk patients (Figure 1). These indicators bear out a close relationship be-

tween lipid metabolic and hemostatic disturbances and between endothelial dysfunction and intracardiac hemodynamic worsening in these patients [13] (Table 1).

Heart rate (HR) at rest is associated with adverse cardiovascular events [14] mainly it is affected due to high LDL/HDL cholesterol levels [15]. LDL cholesterol plays a pivotal role in the formation and clinical expression of atherosclerotic cardiovascular disease. There is an important connection between HDL and immunity in atherosclerosis [16]. LDL is major transporter of cholesterol in the circulation to peripheral tissues and cell membranes. Cholesterol is either reutilized for lipoprotein formation or excreted in the bile. LDL cholesterol is directly related to pathogenesis of atherosclerosis and as a therapeutic target to reduce CVD risks. HDL proteins in the systemic circulation consist of core of esterified cholesterol and triglyceride surrounded by surface monolayer of phospholipid and a range of lipoproteins. The HDL also integrates innate and adaptive immunity because during infections or acute conditions high-density lipoproteins cholesterol levels decrease very rapidly and HDL particles increase [16]. Thus, low HDL cholesterol levels predict severe CVD risks. More often, ability of HDL to influence cholesterol availability in lipid rafts in immune cells results in the modulation of Toll-like receptors, MHC-II complex, and B and T cell receptors, while specific molecules shuttled by HDL such as sphingosine-1-phosphate (S1P) contribute to immune cells trafficking [16]. It has also been tried to correlate lipid abnormalities with hypertension, diabetes, and cardiovascular diseases. Moreover, various cardiovascular risk prediction models have been updated by incorporating traditional risk factors and molecular, immunological genetic, imaging, and biophysical factors for more authentic and reliable estimation of cardiovascular risk. Similarly, myocardial infarction can be assessed by using circulating microRNAs level in patients [17] and Omega-3 Index as a risk factor for cardiovascular diseases [18] (Tables 1).

Thus, risk stratification and assessment of cardiovascular risks in cardiac patients are important areas of research in clinical biology [19]. It warrants further investigations to determine ultramodern emerging risk biomarkers for CVD for more appropriate risk assessment [20] (Figure 1).

Omega-3 polyunsaturated fatty acids (-3 PUFAs) have been shown to have therapeutic potential in a variety of neurological disorders [21]. N-acyl ethanolamines (NAEs) having role in lipid signaling in brain and highlighting multipotential actions on neuronal cell death and neuroinflammatory pathways can become good biomarker for lipid based disorders in several groups of patients [22]

levels of Lp(a) and low HDL cholesterol are also encountered and contribute to the accelerated rate of cardiovascular disease. Cardiac implications are also related to hypoglycaemia in patients with diabetes [23]. Moreover, both type 1 and type 2 diabetes are considered to be high-risk conditions and have stringent cholesterol targets. Similarly, common cholesterol disorders, mainly dyslipidemia, were also found to be specific to the pediatric diabetes population [1] (F. Altered serum lipid level is the most important risk factor for coronary artery disease (CAD) (Table 1).

More often, few proteins such as fat-specific protein (Fsp27), fat storage-inducing transmembrane (FIT) proteins, and seipin and ADP-ribosylation factor 1-coat protein complex I (Arf-COPI) are involved in the regulation of LD formation, expansion, and morphology [24].

Obesity can be cut down by making dietary modification and therapeutic lifestyle changes (TLC). TLC is an effective lifestyle therapy targeting low-density lipoprotein cholesterol (LDL), a risk factor for coronary heart disease. Along with lowering LDL, TLC also improves risk factors associated with the metabolic syndrome and diabetes, including blood pressure, high-density lipoprotein cholesterol (HDL), serum triglycerides, blood glucose, and weight status (Figures 2 and 3). There are so many associating factors which can assist in emerging risks for cardiovascular diseases [25] (Table 1).

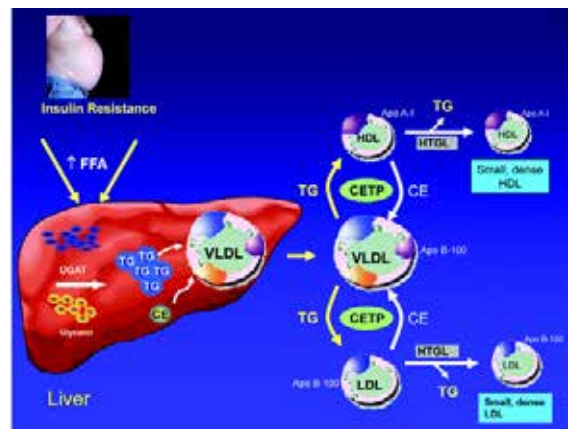
Cardiovascular risks such as defects in angiogenesis/vasculogenesis or vessel repair are major complications of coronary artery disease (CAD) which are mostly seen in aged people. Similarly, CVD risks have also increased in women during pregnancy which is an important issue for management of their cardiovascular health [26]. Cannabis-associated myocardial infarction is observed in young man with normal coronary arteries [27]. In developed countries, there is a large population that shows an increased frequency of atherosclerosis (ATH) mainly systemic lupus erythematosus (SLE). There are paradoxical reports on CAD in South Asian Ethnicity and Cardiovascular Risks [28], but most of atherosclerotic risk factors and atherosclerotic postoperative events are associated with low inflammation in abdominal aortic aneurysms [29]. Similarly, severity of subclinical cardiovascular disease among those with nonalcoholic fatty liver has been alarmingly increased [30] with a significant acute myocardial infarction. Hence, there is an urgent need of potential novel cardiac biomarkers for prediction of acute myocardial infarction [31]. More often, highly sensitive cardiac biomarkers are needed to explore cardiovascular risks, morbidity, and mortality in elderly men [32]. These are also required to predict acute coronary syndrome [33] and for prediction or finding level and type of risk and its assessment in postinfarction heart failure [34] and vasculogenic erectile dysfunction [35]. However, by predicting value of serum soluble ST2 and interleukin-33 are used for risk stratification and prognosis in patients with acute myocardial infarction [36] while circulating biomarkers such as different factors, proteins, ions, stimulators of heart muscles, or deactivators can predict heart failure [37] (Figure 4). Few important body activities such as inflammation, obesity, thrombosis, and autoantibodies also display procardiovascular risks [38] and act as emerging biomarkers [39] (Table 1). Similarly, sedentary behaviour was also proved as an emerging risk factor for cardio-metabolic diseases in children and youth [40].

Hypertension and dyslipidemia are the most prevalent cardiovascular risk factors, with approximately 350 million people having these concomitant conditions throughout globe. Hypercholesterolemia in midlife is related to an increased risk of Alzheimer's disease (AD) in later life. Another possible mechanism, hypercholesterolemia, may be associated with hypoperfusion through the progression of atherosclerosis [41]. Similarly, dyslipidemia is characterized mainly by elevated levels of total cholesterol and low-density lipoproteins in cardiovascular patients. Higher triglyceride levels and lower high-density lipoproteins are encountered 2 and 1.5 times more frequently, respectively. Age-related changes and metabolic hepatic disorders associated with alcohol abuse and consequences of prior infectious diseases play an important role in the pathogenesis of dyslipidemia in patients over 40–45 years of age [42]. Vascular dementia is caused by stroke that occurs due to hypertension. More often for evaluation of lipid related disorders demographic, diagnostic, and medication-related factors are associated with BP (blood pressure) and LDLc goal attainment in patients with concomitant hypertension and dyslipidemia stratified by body mass index BMI. [43] Many more variations were found in therapeutic care in patients with concomitant hypertension and dyslipidemia across different BMI

groups. Further, the presence of high body mass index (BMI) has a negative effect on the achievement of blood pressure (BP) and low-density lipoprotein cholesterol (LDLc) targets. Hence, string markers may be needed for improving these disparities [44]. In addition, concentrations of total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, apolipoprotein A-I, apolipoprotein B, and lipoprotein in serum of patients are biomarkers of primary hypertension and with hyperhomocysteinemia [45] (Table 1).

## 5. Diabetes and Cardiovascular Risks

Cardiovascular disease is more prevalent in type 1 and type 2 diabetes and continues to be the leading cause of death among adults with diabetes. [46] Diabetes coexists as a more severe risk factor with other associating risk factors, in particular with dyslipidemia. [47] It increases cardiovascular risks due to increased levels of triglycerides, low levels of high-density lipoprotein cholesterol, and postprandial lipidemia. Dyslipidemia is mostly observed in patients with type 2 diabetes or metabolic syndrome [48] [49]. In addition, atherosclerotic vascular disease (AVDs) shows obstruction in streaming blood functions due to arterial thickness and high blood pressure. In AVDs, lipid metabolism plays a central role. However, measurement of arterial stiffness provides assessment of endothelial dysfunction and diagnosis of atherosclerotic burden in patients with MetS [50]. Therefore, total serum  $\gamma$ -glutamyl transferase activity (GGT) represents the impact of metabolic disease on vascular injury and atherosclerosis [51]. It acts as important biomarkers of arteriosclerosis in the Multiethnic Study of Atherosclerosis (MESA) Similarly,  $\beta$ -trace protein from GFR marker is also used as cardiovascular risk predictor [52].



**Figure 1: Showing important lipid Fraction in circulation and metabolic disorders related to human cardiovascular disease**

Serum ferritin (SF) level is an important parameter because it has relationship with aggregation of metabolic disorders in nondiabetic elderly patients. Dyslipidemia, obesity, disorders of purine metabolism, and insulin resistance may be important risk factors for higher SF levels in the elderly [53].

ST2, is a member of the interleukin-1 receptor family, is released from cardiac myocytes under mechanical strain. It exists in a transmembrane (ST2L) and a soluble form (sST2) due to alternative splicing. Soluble ST2 (sST2) concentrations are associated with adverse cardiac events in high-risk cohorts. [54]

Gene discoveries have also provided insights into high-density lipoprotein (HDLp) biogenesis and remodeling [55]. More specifically, after advent of genomics main lipid pathways are uncovered and certain modulators or adaptor proteins such as those encoded by LDLRAP1, ApoA5, ANGPTL3/4, and PCSK9 are discovered by genome wide association studies (GWAS). More often, lipid abnormalities and its associated health implications in man have been identified after so many disease responsible genes, its presence on loci, statistical analyses, and functional annotations. These might show large impacts on li-

poprotein traits as gene products that are already known. But importance of new candidate genes is challenging because these may show very low frequencies of large impact variants in the population [56].

### CASE STUDY & CONCLUSIONS

Recent studies it has been come out that in last two-three decades major adverse cardiovascular events (MACE) have been enormously increased. Every year millions of CHD cases are reported in the hospitals but a large number of people that never reach to hospital and expire as unreported. There is hundreds of lipid, carbohydrate, and protein related cardiac dysfunctions which are associated with CHD disease. These are considered as disease favoring factors and also known as emerging risks factors because they indicate presence of some short of cardiovascular dysfunction. Many of these diseases are detected during rehospitalization of patients due to morbidities like unstable angina, heart failure, nonfatal myocardial infarction, arteriosclerosis, and cardiovascular diseases. Besides risk factors there are some faulty dietary consumption like sugar-rich or fat-rich diets which increase CVD risks many fold, because sugar-rich foods are inversely associated with 7 unsaturated long-chain fatty acids. These attribute oxidative stress and impose disordered lipid profiles. In addition, an increased use of drugs, beverages, and sex also induce oxidative stress and contribute to CVD risks.

Atherosclerosis and diabetes are one of the most common disorders among the elderly which are correlated with these factors. Depression is also found to be associated with the development of atherosclerosis and diabetes. Advanced glycation end products play a pivotal role in atherosclerosis [57]. Similarly, inflammation also plays important roles at all stages of atherosclerosis. Inflammation and endothelial dysfunction have been implicated in the pathogenesis of atherosclerotic vascular disease and cause metabolic disturbances like diabetes, atherosclerosis, or metabolic syndrome. Cardiovascular disease (CVD) and Alzheimer disease are significant causes of cognitive impairment in the elderly. Similarly, chronic kidney disease (CKD) is also an independent risk factor for coronary artery disease (CAD). Gene disorders cause acute coronary syndrome (ACS) and need one of the most frequent differential diagnoses in emergency medicine.

More often, atherosclerotic peripheral arterial disease (PAD) is one of the most prevalent, morbid, and mortal diseases. Chemokines play important roles in atherosclerotic vascular disease. These have major effects on the initiation and progression of atherosclerosis by controlling the trafficking of inflammatory cells in vivo through interaction with their receptors. Long-term intake of long-chain n-3 polyunsaturated fatty acids (n-3 PUFAs), especially eicosapentaenoic acid (EPA), is associated with a low risk for cardiovascular disease. It is well known that people with high levels of body fat remain at higher risk for developing diabetes mellitus, kidney disease, and cardiovascular disorders. Since individuals who are slightly overweight, or even individuals of normal weight, can vary in body fat distribution, their metabolic profiles and the degree of association of these profiles with cardio metabolic risk factors may differ. The regional fat distribution may play a key role in understanding the development of cardio metabolic diseases in non-obese people [58]. Hence, fat consumption or extreme calorie consumption burning by passing through an aerobic exercise provides some relief, defeating drugs. In addition, high fat intake in diet should be avoided by all categories of people because it shows long-term effects and evokes obesity genes.

A large number of novel biomarkers that reflect a broad range of pathological events involved in the progression of atherosclerosis have been reported in association with cardiovascular risk. Moreover, LDL cholesterol level, HDLp and apolipoprotein levels, lipophorins and LTPs ratio, sphingolipids, Omega-3 Index and ST2, immunohistochemical, oxidative stress, inflammatory, anatomical, imaging, genetic markers, and therapeutic biomarkers are proved to be much better for clinical diagnosis

of CVDs. Further, assessment of global risk may require integration of multiple biomarkers reflecting the different pathological pathways involved in atherosclerosis. Hence, all risk factors which can assist in incremental risk prediction must be included in diagnosis, to tailor therapy or to monitor the effects of therapy in a cost-effective manner. Each of the pathological pathways involved in the generation and subsequent rupture of atherosclerotic plaque might theoretically reveal systemic markers that may be of utility in risk prediction and in monitoring the response to therapy. Additional markers of oxidative stress may be of high utility if developed. Systemic levels of the MPO products, chlorotyrosine, and nitrotyrosine and use of statin were found to be the best therapeutic biomarkers for best cardioprotective measures. In addition, various metabolites of arachidonic acid can be measured in both blood and urine and have been reported as associated with cardiovascular risks. In the cardiovascular system, miRNAs not only impact on physiological pathways like cardiac development and angiogenesis, but also play an important role in disease mechanisms and progression of myocardial hypertrophy, acute myocardial infarction, heart failure, or arrhythmias. Hence, an association between inflammatory markers and future HF risk in patients with stable CAD needs further explorations for finding possible solution of myocardial infarction (MI) in man. Other inflammatory markers such as interleukin-1 receptor-1 (IL1R1) and its ligand, IL1, are upregulated in cardiovascular disease, obesity, and infection. Apo lipoproteins are very heterogeneous protein family, implicated in plasma lipoprotein structural stabilization, lipid metabolism, inflammation, or immunity. However, by measuring serum and plasma lipoproteins, their components and lipid profile of patients may not only predict occurrence of CVDs based on lipoprotein roles in atherogenesis but also help in development of new therapeutic strategies for the treatment of lipoprotein-associated disorders. Thus, improving the quality of HDL may represent a better therapeutic target than simply raising the HDL level and assessment of HDL function may prove informative in refining our understanding of HDL-mediated atheroprotection. Metabolomics may reveal novel metabolic biomarkers of dietary intake and provide insight into biochemical pathways underlying nutritional effects on disease development.

Lipid disorders are also the risk factors for CVDs. Therefore, an earlier diagnosis and treatment are necessary to prevent different types of lipid abnormalities and to predict emerging risks of various cardiovascular diseases and disorders. There is a need to prepare a detailed metabolic calendar for daily dietary use to minimize the CVD risks in patients. More specifically obesity-induced perturbations in metabolic function should be checked from time to time. Though dietary lipid abnormalities can be reversed by changing the food habits, exercise, and use of fat mobilizing drugs and replacement therapy, genetic abnormalities are not possible to restore them immediately and need effective control measures with proper clinical care. It is an important issue which is directly related to public health. Hence, combined efforts are needed to develop and explore new risk biomarkers for an accurate and proper disease diagnosis. In addition, more sophisticated therapeutic markers are also needed for achieving good therapeutic targets. Conclusively this huge target could not be achieved without making integrating efforts made by biochemists, immunologists, molecular biologists to unfold the mystery of CVDs, its more accurate diagnosis, and therapeutics as well.

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