MEDWIN PUBLISHERS
Committed to Create Value for Researchers

International Journal of Biochemistry & Physiology
ISSN: 2577-4360

Biochemical and Pathological Parameters Pertaining to Cardiovascular Disorders

Sanjay Mishra[1]*, Amit Mani Tiwari[2] and Priyanka Nayak[3]

[1]Department of Biotechnology, SR Institute of Management & Technology, India
[2]Department of Biotechnology, Era University, India
[3]Regional Food Research & Analysis Centre, India

***Corresponding author:** Dr. Sanjay Mishra, Professor, Department of Biotechnology, SR Institute of management & Technology, Uttar Pradesh, India, Tel: 9837096059; Email: sanjaymishra66@gmail.com

Editorial
Volume 9 Issue 1
Received Date: February 02, 2024
Published Date: February 09, 2024
DOI: 10.23880/ijbp-16000241

Abbreviations: MS: Metabolic Syndrome; NCDs: Non-Communicable Diseases; ASCVD: Atherosclerotic Cardiovascular Disease.

Editorial

Metabolic syndrome (MS) has become the major health hazard of modern world among all non-communicable diseases (NCDs) and mainly feeds into the spread of the diseases like type-2 diabetes (T2DM) and atherosclerotic cardiovascular disease (ASCVD) [1]. NCD linked deaths around the world, one-fourth of them result from arterial blockage caused by atherosclerotic plaques and ASCVD characterized by occlusion of the coronary arteries leading to heart attacks. Moreover, annual deaths attributed to T2DM have also been estimated to climb by 38% till 2030. Contrariwise, in India, cardiovascular diseases contributed about 28% of the total deaths and 14 % of the total disability-adjusted life-years (DALYs) in 2016 compared with approximate 15% and 7%, respectively in 1990 [1]. Among various risk factors, variation in lipoproteins, cholesterol and triglyceride levels are highest driver of onset of ASCVD, enabling it the prime target for ASCVD risk reduction. However, hepatic LDL receptors (LDL-R) are the vital mediators connected with clearance of more than 70% of LDL-c present in the circulation. Recently, the protein lipoprotein convertase subtilisin/kexin type 9 (CPSK-9) has emerged as a foremost drug target in cardiovascular medicine and pharmacology. PCSK-9 directly binds to the EGF-A domain of LDL-R which in turn blocks LDL-R recycling via its lysosomal degradation [2].

In addition to the classical risk factors, distinct genetic polymorphism studies concluded that genetic variants/ mutations in genes involved in cholesterol biosynthesis, cholesterol transport and cholesterol metabolism (i.e. PCSK-9 & LDL-R) have also been found to be involved in ASCVD and T2DM pathogenesis. The GOF mutations in a high rate of LDL-T degradation, whereas LOF mutations that inactivate PCS-9 will lead to low levels of plasma LDL-c. Also, the enhanced expression of PCSK9 has been linked to reduced surface LDL-R [3]. The rs505151 polymorphism in PCSK9 resulted in an increased affinity of PCSK9 for the LDL-R and hence the altered LDL-c levels. Many studies extrapolated the association of PCSK9 and LDL-R polymorphisms with LDL-c but ended with contradicting effects. Besides, hepatic β-hydroxy-β-methyl-glutaryl-CoA reductase (HMG-R) is the chief cholesterogenic enzyme that maintains the cholesterol homeostasis in vivo. HMG-R inhibitors, statins are the most extensively prescribed medication against ASCVD and they also protect against disorders. Atherosclerosis is a progressive disorder of arteries with varying sizes characterized by the formation and calcification of atheromatous plaques in the arteries vessel walls. The atherosclerosis process is initiated by lipid peroxidation and oxidative modifications inside the arteries intima, which provoke chronic inflammation cascades, ultimately causing thrombosis and plaque formation. Although lesions begin in the intima, the inner lining of arteries, they later affect the other constituent layers of arterial wall including the media and the adventitia [4,5].

Numerous studies in animal models as well as human have been established that the fatty streaks are the first

sign of atherosclerosis. The initial lesions are usually caused by the entrapment and focal increase of the lipoproteins beneath the initial layer of the arteries. These lipoproteins are composed of proteins, phospholipids and also lipids such as cholesterol and triglycerides, fatty steak formation [6,7].

The first step in atherosclerosis is the trapping of the lipoproteins in the lesion site. Among distinct lipoproteins, LDL has been thought to be the principle atherogenic lipoproteins due to its ability to accumulate in the arterial wall following its infiltration into the endothelium or adherence to extracellular matrix components like proteoglycan [8]. Although, LDL-C cannot pass through the tight endothelial junctions, it can rapidly enter the endothelial cells (ECs) through endocytosis. As per level of plasma LDL rises, many of these particles are trapped in the intima.

Although the endothelial barrier consists of only a single layer of ECs, its participation in the development of atherosclerosis is very crucial. Activation of ECs is characterized by endothelial expression of cell surface adhesion molecules such as intracellular adhesion molecule-1 (ICAM-1) and vascular adhesion molecule-1 (VCAM-1), P-selectin and E-selectin which is also known as the endothelial leukocyte adhesion molecule (ELAM) [9]. Pro-inflammatory cytokines such as tumor necrotic factor-α, and interleukin (IL-6) together with oxidized LDL (Ox-LDL) play crucial roles in the activation of endothelial cells. In addition, nuclear factor-κB (NF- κB) signaling cascade have also been established as the major cause of endothelial activation. Recent studies have confirmed that Ox-LDL receptor, which ultimately facilitates the uptake of this Ox-LDL into the activated human endothelial cells. Ox-LDL is also known to trigger the expression of ICAM-1 and VCAM-1 in ECs which potentiates the process of cellular requirement in the arteries through the activation of inflammatory cascade [9].

Activation and migration of leukocytes into the vessel wall is among the key pathological events in the progression of atherosclerosis. Various leukocytes including monocytes, neutrophils and T lymphocytes infiltrate into vascular intima under the influence of oxidative stress and inflammatory environment. Ox-LDL also activates T cells as it is considered an antigen by T cells and leads to the cytokines secretion which ultimately impacts the functionality of leukocytes. The activation of leukocytes is facilitated by the expression of leukocyte and chemokine adhesion molecules by the sites of inflammation and local tissue resident cells. These adhesion molecules are recognized by their receptors that are expressed by the specific leukocytes, vascular smooth muscle cells (VSMCs) or vascular ECs. Moreover, specific chemokines cause endothelial and SMCs to migrate. Monocytes chemokine protein (MCP-1) is expressed considerably by macrophages and in a less amount by SMCs and endothelial in all steps of atherosclerosis. High level of MCP-1 attracts monocytes towards the vascular walls and promotes their infiltration into the endothelial lesion and subsequent transformation into macrophages. Ox-LDL has also been reported to trigger the expression of various chemokines including IL-1α, IL-1β, IL-6, chemokine (C-X-C motif) ligand-1 and -2 and MCP-1 in ECs [10].

Mononuclear phagocytes, particularly monocytes, differentiate into macrophages when enter in the intima. These macrophages phagocytize trapped lipids including Ox-LDL to form foam cells. This process is strictly regulated by the expression of distinct surface receptors expressed by phagocytes for elimination of different molecules and inflammatory cytokines from the damaged endothelium [11]. The monocytes that do not form foam cells secrete cytotoxic substances like TNF, growth factors, pre-coagulation substances and highly reactive free radicals leading to comparatively greater damage to endothelial barrier as well as extensive LDL oxidation leading to further and accelerate endothelial dysfunction. This sequential process from entrapment of LDL to the accumulation of fat laden foam cells in the arterial walls is collectively known as the formation of fatty streaks [12].

An atheroma, is an abnormal accumulation of material in the arterial wall. The material consists of mostly cholesterol, various leukocytes, inflammatory cells, cell debris, calcium and a variable amount of fibrous connective tissues [5]. The material causes a swelling in the arterial wall which narrowing of arteries and restricting blood flow. Subsequent secretion of cytokines and growth factors by SMCs and ECs leads to the severe damage to vascular tissues and also promotes SMCs migration towards intima. These SMCs together with extracellular matrix participate in the formation of fibrous cap, composed of collagen-rich fibrous tissues, SMCs, macrophages and T-lymphocytes [5,13]. A collective mass of these materials is reckoned as atherosclerotic plaque and macrophages and T-lymphocytes align themselves towards its borders to give it a projection like shape which produces obstructions in blood stream in the vessel by narrowing the vessels. Macrophages and SMCs secrete distinct proteolytic enzyme including matrix metalloproteinases (MMPs-1, 2, 8 & 13) with the capability to lyse extracellular matrix, particularly collagen type I and III, which reduces the strength of fibrous cap and plaque plasticity and ultimately leads to the plaque rupture. Plaque rupture exposes damaged collagen and lipids to blood stream which contributes to blood clot formation and may suddenly block the blood stream. Many foam cells in intima die through apoptosis leaving a lipid rich necrosis nucleus in the center of more developed atherosclerotic plaque [13].

A large number of emerging novel biomarkers are known but none of the existing biomarkers for cardiovascular disease are routinely castoff and precisely validated among the population and do not appear in cardiovascular risk; however, the roles and biochemistry of these markers as they relate to the risk of future cardiovascular events in individuals with and without CAD and their clear clinical utility have not yet been fully elucidated [14]. Accordingly, it is difficult to draw specific conclusions from the current evidence regarding the mechanisms through which a biomarker could affect the prognosis. Although there is evidence that combining biomarkers may increase the accuracy of certain tests, the optimal combinations for diagnosis or prognosis need to be defined.

Taken together, all these papers underline the need to have simple, cost-effective and easily available biomarkers for the diagnosis and follow-up of CVD. The wide number of biomarkers investigated in this Research Topic can help physicians now and in the near future to better manage CVD, highly impacting on patient's prognosis as well as quality of life.

Conclusion and Future Perspectives

Conclusively, none of the existing biomarkers for cardiovascular disease are routinely used and scientifically validated among the overall population and do not appear in cardiovascular risk scores till last decade. Although several types of antihyperlipidemic drugs have been introduced to the market and are actively applied in clinical practice [15], they are not devoid of drawbacks such as well-known side effects (statins) or high costs (monoclonal antibodies). Thus, there is still a need for effective cholesterol-lowering drugs with minimal side-effects, preferably orally bioavailable. The low-molecular PCSK9 inhibitors would be a worthy alternative for this purpose. Besides, certain component pathologies of the metabolic syndrome contribute to a higher percentage of total oxidative stress than others; nevertheless, additional studies are obligatory to conclude the precise role of individual constituents to entire oxidative stress. Nevertheless this editorial provides new insights into exploring the platform to further expand biochemical and pathological parameters linking to cardiovascular disorders.

Acknowledgement

Contributors of this 'Editorial' duly acknowledge Chairman Mr. Pawan Singh Chauhan, Vice Chairman Mr. Piyush Singh Chauhan, Board of Directors and Head, Department of Biotechnology of S.R. Institute of Management and Technology, Lucknow, U.P., India for the throughout motivation to expand the platform of research and development.

References

1. Mishra S, Tiwari AKM, Mahdi AA (2017) Physiological biochemical and molecular role of oxidative stress in cardiovascular disease A comprehensive study. Current Research in Cardiovascular Pharmacology 6 (1): 1-16.

2. Holmes MV, Millwood IY, Kartsonaki C, Hill MR, Bennett DA, et al. (2018) Lipids lipoproteins and metabolites and risk of myocardial infarction and stroke. J Am Coll Cardiol.71(6): 620–632.

3. Barale C, Melchionda E, Morotti A, Russo I (2021) PCSK9 biology and its role in atherothrombosis. Int J Mol Sci 22(11): 5880.

4. Mishra S, Dwivedi SP, Singh RB, Shastun S, Abramova M (2015) Role of oxidative stress in the pathogenesis and progression of coronary artery disease An overview. World Heart Journal 6(4): 283-302.

5. Jebari BS, Galicia GU, Larrea SA, Olaetxea JR, Alloza I, et al. (2022) Pathophysiology of atherosclerosis. Int J Mol Sci 23(6): 3346.

6. Zhang B, Gu J, Qian M, Niu L, Zhou H, et al. (2017) Correlation between quantitative analysis of wall shear stress and intima-media thickness in atherosclerosis development in carotid arteries. Biomed Eng Online 16(1): 137.

7. Sun HJ, Wu ZY, Nie XW, Bian JS (2020) Role of Endothelial Dysfunction in Cardiovascular Diseases: The Link Between Inflammation and Hydrogen Sulfide. Front Pharmacol 10: 1568.

8. Boren J, Chapman MJ, Krauss RM, Packard CJ, Bentzon JF, et al. (2020) Low-density lipoproteins cause atherosclerotic cardiovascular disease: pathophysiological genetic and therapeutic insights a consensus statement from the European Atherosclerosis Society Consensus Panel. Eur Heart J 41(24): 2313-2330.

9. Vielhauer V, Stavrakis G, Mayadas TN (2005) Renal cell-expressed TNF receptor 2 not receptor 1 is essential for the development of glomerulonephritis. J Clin Invest 115(5): 1199-1209.

10. Chandrasekharan UM, Siemionow M, Unsal M, Yang L, Poptic E, et al. (2007) Tumor necrosis factor α (TNF- α) receptor-II is required for TNF α induced leukocyte-endothelial interaction in vivo. Blood 109 (5): 1938-1944.

11. Lorey MB, Oorni K, Kovanen PT (2022) Modified lipoproteins induce arterial wall inflammation during

atherogenesis. Front Cardiovasc Med 9.

12. Jang E, Robert J, Rohrer L, Eckardstein A, Lee WL (2020) Transendothelial transport of lipoproteins. Atherosclerosis 315: 111-125.

13. Campinho P, Vilfan A, Vermot J (2020) Blood Flow Forces in Shaping the Vascular System A Focus on Endothelial Cell Behavior. Front Physiol 11: 552.

14. Wang J, Tanz GJ, Han LN, Yong Yi, Bai YY, et al. (2017) Novel biomarkers for cardiovascular risk prediction. J Geriatr Cardiol 14(2): 135-150.

15. Kuzmich N, Andresyuk E, Porozov Y, Tarasov V, Samsonov M, et al. (2022) PCSK9 as a Target for Development of a New Generation of Hypolipidemic Drugs. Molecules 27(2): 434.