ENDOTHELIAL DYSFUNCTION: A CARDIOVASCULAR RISK FACTOR

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ABSTRACT
Endothelium is one of the largest organ by area and consist of at least one trillion endothelial cells having more than 100 gram weight and covering more than 3000 square meters area in an adult human body. Endothelium interacts with most of the body systems and is implicated in end organ diseases particularly the cardiovascular. The endothelium maintains vascular tone by precisely regulating the vasodilatation and vasoconstriction while effectively providing the adequate supply of blood to the target organs. Factors that affect the endothelium and subsequently cardiovascular system include hypertension, smoking, obesity, hyperglycemia, hyperlipidemia, poor dietary habits and physical inactivity. Endothelial dysfunction is strongly associated with cardiovascular risk factors such as atherosclerosis, elevated level of low density lipoprotein oxidation, cytokine elaboration, up regulation of adhesion molecules, increased cell permeability, platelet aggregation as well as proliferation and migration of vascular smooth muscles. Endothelial dysfunction is a pathophysiological term used to indicate diminished production of nitric oxide and an imbalance in endothelial derived contraction and relaxation.

KEY WORDS: Endothelium; Endothelial cells; Endothelial dysfunction; Atherosclerosis; Hyperglycemia; Hyperlipidemia; Nitric oxide; Reactive oxygen species; Diabetes mellitus; Hypertension.


INTRODUCTION
The vascular endothelium is a monolayer of endothelial cells forming the inner lining of all blood vessels including arteries, veins and capillaries as well as lymphatic system. The endothelium is autocrine, paracrine and endocrine organ regulating the vascular tone and maintain the homeostasis.¹² The pathophysiological alteration of endothelium results in the endothelium dysfunction, leading to atherosclerosis and plaque formation. It may subsequently lead to imbalance in vasoconstriction and vasodilatation which are associated with an increased risk of cardiovascular disorders.¹²

The endothelial dysfunction results in decreased bioavailability of vasodilators, specifically the nitric oxide (NO). It also causes increased level of endothelium-derived contractile factors.³ This imbalance may lead to the impairments of endothelium-dependent vasodilatation resulting into proliferation, inflammation and coagulation, associated with cardiovascular events.⁴

The cardiovascular risk factors include hypertension, smoking, hyperglycemia, aging, hypercholesterolemia and a family history of atherosclerotic diseases which are concomitant with endothelial dysfunction and cardiovascular disorders.⁵⁻⁷ These factors are strongly associated with inflammation, thrombosis, vasoconstriction, elevated level of C-reactive protein as well as systemic infections, contributing to cardiovascular events (Figure 1).⁸⁻¹⁰

Keeping in view the direct relationship between endothelial dysfunction and atherosclerosis, the diseased status of endothelium is directly involved in the pathophysiology of various cardiovascular disorders including hypertension, inflammation, generation of reactive oxygen species (ROS), oxidative stress and other vascular abnormalities such as coronary heart disease and pulmonary hypertension. Here in this review we have summarized the literature regarding endothelial dysfunction and cardiovascular disorders.
Endothelial dysfunction plays a vital role in the pathogenesis of acute coronary syndrome. The endothelium is involved in the plaque destabilization with reactive oxygen species (ROS), a central promoter of inflammatory processes. For the diagnosis of coronary endothelial functioning, the noninvasive tests such as Doppler echocardiography (ECHO), phase-contrast magnetic resonance imaging (PMRI) and positron emission tomography (PET) are used. Moreover, the gold standard and invasive test is the intracoronary Doppler techniques to measure the coronary blood flow in response to a physiological or pharmacological stimuli. The diabetes induced endothelial dysfunction is also associated with an increased risk of cardiovascular events in hyperglycemia. The intracellular depletion of NADPH occurs as a result of redox reaction. In diabetes the overexpression of growth factors have also been reported which results both in the proliferation of endothelial cells and vascular smooth muscles, probably promoting the neovascularization. The non-enzymatic glycation of the macromolecules including proteins are also associated with chronic diabetes.

The diabetic patients have an increased tendency towards oxidative stress resulting in increased level of oxidized lipoprotein particularly the low density lipoprotein (LDL). In case of hyperglycemia and high level of fatty acids, oxidation of phospholipids and proteins has also been reported that may result in the platelet aggregation and prothrombotic tendency. Insulin resistant diabetes are implicated with endothelial dysfunction, supported by the hypothesis "insulin and/ or insulin precursor may be atherogenic."

Thoroughly investigating the literature, it has been
revealed that the diminished concentration of NO synthase to produce NO has been associated with endothelial cells when placed in an in vivo diabetic environment. Most of the experimental studies reported that endothelial dysfunction is closely related with atherosclerosis and microangiopathy in diabetes.

CONCLUSION
Dysfunctioning endothelium is the leading cause of various cardiovascular events including hypertension, coronary heart diseases, atherosclerosis, platelet aggregation and so many similar events.

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All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.