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REVIEW ARTICLE

Air Pollution: A leading Risk Factor for Coronary Artery Disease

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ABSTRACT

Air pollution is one of the leading potent environmental problem in the modern world for all living creatures. It produces multiple health hazards like cardiovascular dieseses, respiratory diseases and skin diseases. However, air pollution is emerging as a leading risk factor for coronary artery disease. It promotes oxidative stress, systemic inflammation, autonomic dysfunction, metabolic dysregulation, hypercoagulability, and epigenetic changes. Individuals with genetic susceptibility face compounded risks, underscoring the need for personalized and public health interventions. Through a combination of behavioural, public awareness, medical and policy-driven strategies, the burden of air pollution-induced coronary artery disease can be significantly reduced.

KEYWORDS

• Air Pollution • Coronary Artery Disease • Particulate matter • Public health implication

INTRODUCTION

Coronary artery disease (CAD) emerges as a big health burden, responsible for significant morbidity and mortality. The disease is influenced by both genetic susceptibility and atmospheric exposures. Air pollution is surfacing as a critical but modifiable risk factor in India and the world. Particulate matter (PM2.5, PM10), nitrogen dioxide (NO_2), nitrogen oxides (NOx), sulphur dioxide (SO_2), carbon monoxide (CO), and ozone (O_3) are pollutants that have been linked to cardiovascular dysfunction. These have been

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found to cause oxidative stress, endothelial dysfunction, autonomic derangement, metabolic alterations, systemic inflammation response and hypercoagulability in various studies.[1]

Epidemiological studies and data from the UK Biobank highlight that polygenic risk scores (PRS) can be used to evaluate the interaction between genetic predisposition and air pollution in the onset of CAD and myocardial infarction. These studies suggest a positive additive gene-environment interaction, emphasizing that individuals with a high genetic risk for CAD may experience greater susceptibility to air pollution-induced cardiovascular damage.[1]

Epidemiological Evidence Linking Air Pollution to CAD

From a systematic review of 2,884 individual citations, 26 eligible studies had examined the relationship between air pollution and cardiac function and found a negative association between air pollutants and cardiovascular health, particularly affecting heart rate variability (HRV), a key measure of autonomic function, in a majority (18 out of 22 studies (82%) of participants. 10 out of 13 studies, in the same systematic review, demonstrated significant reductions in HRV indices following air pollution exposure, although beta-blocker use appeared to moderate some of these effects.[2]

Additionally, increased hospitalizations, readmissions, and premature mortality among CAD patients has been linked to air pollution.[3] Specific pollutants such as PM1, PM2.5, ultrafine particles (0.01–0.1 μm), black carbon, diesel exhaust and SO2 have been linked to increased ST-segment depression in CAD patients, indicating myocardial ischemia.

Electrocardiographic (ECG) abnormalities, including prolonged PR, QRS, and QT intervals and increased heart rate lasting up to seven days post-exposure.

Increased risk of ventricular arrhythmias in patients with implantable cardioverter defibrillators (ICDs).[4]

Ultrafine particles, PM2.5 and AMP (Accumulation Mode Particles) have been associated with systolic hypertension (by up to 0.94 mmHg).[5]

Furthermore, air pollution has been shown to attenuate the cardiovascular benefits of exercise. A recent study found that adults with ischemic heart disease who exercised in polluted environments experienced a significantly lower improvement in vascular function compared to those who exercised in non-polluted urban parks.[3]

Pathophysiological Mechanisms Linking Air Pollution to CAD

1. Oxidative Stress and Endothelial Dysfunction

Of the many mechanisms postulated, by which air pollution contributes to CAD, oxidative stress, was found to cause endothelial dysfunction, vascular inflammation, and accelerated atherosclerosis.[6,7,8]

Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS): PM2.5 exposure promotes ROS and RNS production, disrupting cellular mechanisms such as NADPH oxidases (NOXs), endothelial nitric oxide synthase (eNOS) uncoupling, and mitochondrial respiratory chain dysfunction.[9]

eNOS uncoupling results in the formation of superoxide radicals, leading to peroxynitrite ($ONOO^-$) production, which oxidizes lipids and proteins, further damaging the endothelium.[10]

Oxidized LDL (ox-LDL) and Atherosclerosis Progression: $ONOO^-$ radicals oxidize circulating low-density lipoprotein (LDL) to ox-LDL, which activates lectin-like oxidized low-density lipoprotein receptor-1 (LOX-1). LOX-1 activation leads to:

Intimal thickening due to vascular smooth muscle cell (VSMC) proliferation.

Increased extracellular matrix deposition, accelerating vascular remodeling.[10]

Role of Heavy Metals in Air Pollution: Highly reactive hydroxyl radicals that exacerbate oxidative damage are produced by Fenton reactions that are catalysed by metals present on the surface of PM2.5 particles.[11]

2. Inflammation and Systemic Immune Activation

Air pollution exposure triggers systemic inflammation, a key driver of atherosclerosis.

Increased Inflammatory Markers:

Increased levels of C-reactive protein (CRP), plasma fibrinogen, and pro-inflammatory cytokines (TNF-α, IL-6, IL-1β) have been

associated with PM2.5 exposure.

Chronic inflammation promotes the recruitment of monocytes and macrophages, leading to plaque formation and instability.

Leukocyte and Endothelial Activation: PM2.5 activates circulating leukocytes and endothelial cells, increasing the expression of adhesion molecules (ICAM-1, VCAM-1, E-selectin), which facilitate monocyte migration into the arterial wall.

This process promotes the formation of foam cells, which is a hallmark of atherosclerotic plaque development.[12]

3. Autonomic Dysfunction and Neuroendocrine Imbalance

Air pollution disrupts the autonomic nervous system, increasing sympathetic nervous system activity while reducing parasympathetic tone[13], leading to:

Increased blood pressure and heart rate, exacerbating myocardial oxygen demand.

Vasoconstriction and endothelial dysfunction, impairing coronary circulation.

Pulmonary Reflex Activation:

PM2.5 stimulates transient receptor potential (TRP) channels in the lungs, activating neural reflex arcs that increase systemic sympathetic output and catecholamine release.[14]

4. Metabolic Dysregulation and Lipid Alterations

PM2.5 exposure induces a unique form of dyslipidemia, characterized by:

Increased LDL, ox-LDL, triglycerides, and lipoprotein(a).

Decreased HDL and apolipoprotein A1, impairing reverse cholesterol transport.

Inflamed atherosclerotic plaques that are lipid-rich develop due to this metabolic shift.[15]

5. Hypercoagulability and Thrombosis

Air pollution increases the risk of thrombosis through several mechanisms[16]: Elevated coagulation biomarkers: Increased levels of fibrinogen, thrombin, plasminogen activator inhibitor-1 (PAI-1), tissue plasminogen activator (tPA) and von Willebrand factor.

Platelet activation and aggregation: PM2.5 increases risk of acute coronary events by enhancing platelet adhesion and thereby reducing clotting time.

6. Epigenetic Reprogramming and Genetic Susceptibility

PM2.5 exposure induces histone modifications (H3K9 acetylation, H3K27 tri-methylation), which correlate with increased blood pressure, vascular inflammation, and atherosclerosis progression.[17]

MicroRNA (miRNA) dysregulation affects cytokine production, exacerbating vascular inflammation.[18]

Mitochondrial dysfunction: PM2.5 exposure damages mitochondrial DNA (mtDNA) and impairs electron transport chain function resulting in oxidative stress and endothelial dysfunction.[19]

Clinical and Public Health Implications

Given the strong evidence linking air pollution to CAD, strategies to mitigate exposure include:

i) ***Monitoring Air Quality:*** Individuals, especially those with CAD, should track air pollution levels and limit outdoor activity during high pollution periods.

ii) ***Personal Protective Measures:*** Use of N95 masks, air purifiers, and indoor filtration systems can reduce exposure. Lifestyle Interventions: Healthy diet, exercise in low-pollution environments, and adherence to medications can mitigate risks.

iii) ***Policy Changes:*** Governments must enforce stricter emissions regulations for industry, construction works and automobiles, promote clean energy, and expand urban green spaces.

iv) ***Citizen contribution:*** Increasing public awareness for hazards of air pollution, stopping stable burning, improving cleanliness, expanding indoor and outdoor gardening and use of LPG, CNG and other cleaner fuel alternatives.

CONCLUSION

Air pollution is a leading potent environmental risk factor for coronary artery disease. Air pollution promotes oxidative stress, systemic inflammation, autonomic dysfunction, metabolic dysregulation, hypercoagulability, and epigenetic changes. Individuals with genetic susceptibility face

compounded risks, underscoring the need for personalized and public health interventions. Through a combination of medical, behavioural, and policy-driven strategies, the burden of air pollution-induced cardiovascular disease can be significantly reduced.

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