The In-Depth Relationship between Air Pollutants and Coronary Artery Disease in South Asia: A Review

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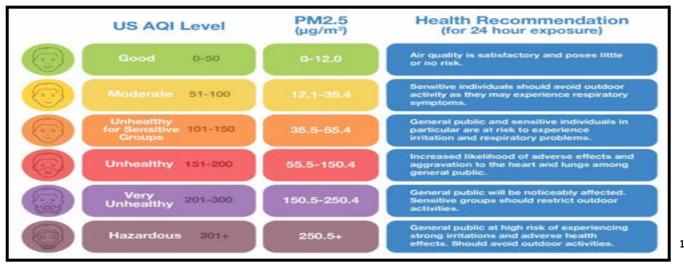
ABSTRACT

Coronary artery disease (CAD) is a potentially fatal cardiovascular condition characterized by the obstruction of plaque, disrupting appropriate blood flow to the heart. While the buildup of cholesterol deposits is a common cause of CAD, new research by Roopesh Singh Gangwar^[1] has shown that reactive oxygen species (ROS) created from exposure to Particulate Matter 2.5 (PM 2.5) can also contribute to the disease. In South Asia, air pollutants such as PM2.5 and methane combustion are at extreme levels and have been firmly associated with the development of cardiovascular disease. Specifically, Pakistan's most common heart disease is CAD, and cardiovascular disease is the leading cause of death^[2]. The country has experienced pollutant levels above 35 μ g/m³, which are considered detrimental to human health. Although the negative impacts of PM2.5 are not completely understood scientifically, recent studies by Prakash Thangavel^[3] have pointed to connections with ROS. This paper will discuss the correlation between elevated PM2.5 and ROS levels and the increased rates of cardiovascular disease in the most affected provinces of South Asia, as well as the impact of other industrial pollutants such as volatile organic compounds (VOCs) and methane.

<u>Key terms</u>: Coronary Heart Disease, PM2.5, Oxidative stress, ROS, Volatile Organic Compounds, Systemic Inflammation

INTRODUCTION

In 2022, among the ten most air-polluted cities in the world, nine were located in South Asia, according to Smart Air^[4]. Global air pollution is a serious concern, and if countries do not adopt sustainable practices, the issue will only worsen.



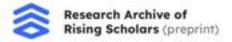
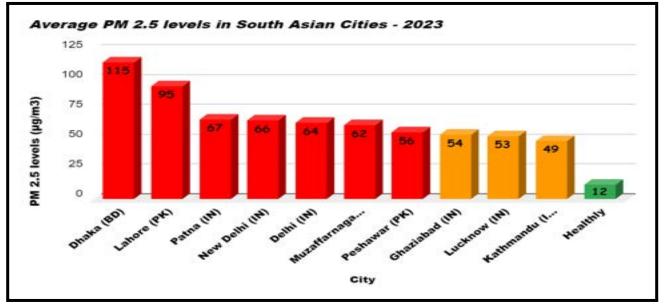


Figure 1: Chart illustrating the US AQI levels, corresponding PM2.5 concentrations, and associated health recommendations for 24-hour exposure. Each level includes specific health recommendations, such as sensitive individuals avoiding outdoor activity at the Moderate level, and the general public restricting outdoor activities at the Very Unhealthy level. Graph created by AQI Basics.

The Air Quality Index (AQI) measures how polluted or clean the air is in an area, using pollutants such as ozone, carbon monoxide, particulate matter, sulfur dioxide, and nitrogen dioxide. The AQI is calculated based on concentrations of multiple pollutants measured over a specific time period at monitoring stations. Governments and environmental organizations use the AQI to inform the public about air quality conditions. The AQI typically includes six levels, each representing different air quality conditions: Good (0-50), Moderate (51-100), Unhealthy for Sensitive Groups (101-150), Unhealthy (151-200), Very Unhealthy (201-300), & Hazardous (301-500)^[4]. The 0-50 range indicates satisfactory air quality with little to no health risks. The 51-100 range is acceptable but may pose health concerns for some individuals, including those with respiratory or heart issues. The 101-150 range indicates that people with respiratory or heart conditions, children, and older adults may experience health effects, while the general public is less likely to be affected. The 151-200 range is hazardous, with everyone potentially experiencing adverse health effects, especially sensitive groups. The 201-300 range involves health warnings of emergency conditions, affecting the entire population. The 301-500 range is hazardous, with serious health effects for those affected^[5].

PM2.5, or particulate matter with a diameter of 2.5 micrometers or smaller, has been linked to a range of health problems, including respiratory issues such as asthma, bronchitis, reduced lung function, and cardiovascular disease^[6]. Although PM2.5 isn't a greenhouse gas, prolonged exposure can cause significant health effects. The image below shows the top ten highest average PM2.5 levels in South Asia. Notably, a healthy level for humans is 12 μ g/m³, but many of these countries have treacherous PM2.5 levels noticeably above normal levels.



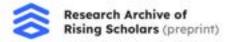


Figure 2: Bar Graph depicting the top 10 highest average rates of PM2.5 levels in cities globally. The X-axis represents the cities, and the Y-axis depicts the average AQI level. As shown, most South Asian cities are on this list and ranked among the top polluted cities in the world. The polluted cities are far above the healthy level (100 AQI), which could correlate with coronary artery disease in South Asian countries. Data from Smart Air. Bar Graph created by Shashwat Mishra.

Air pollution is soon becoming a national health emergency in India once again following the slight decrease in such levels as result of the covid-19 lockdown^{[7][8]}. Now, the issue at hand is very much present, however the nation is unable to effectively combat its sustainability at a large scale. Individuals with health issues such as worsened asthma are particularly vulnerable to the effects of air pollution and those in these areas are already largely experiencing the detrimental effects^[8]. This too, considering Indians are already very predisposed to asthma, even holding 14 percent of the global asthma burden^[9].

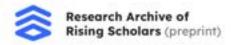
Along with this, provinces in South Asia also have extremely high levels of coronary artery disease fatalities^{[10][11]}. The remainder of the article will meticulously elucidate the characteristics and biological/anatomic impacts of certain air particles on the emergence of cardiovascular disease, as well as their relation to South Asia.

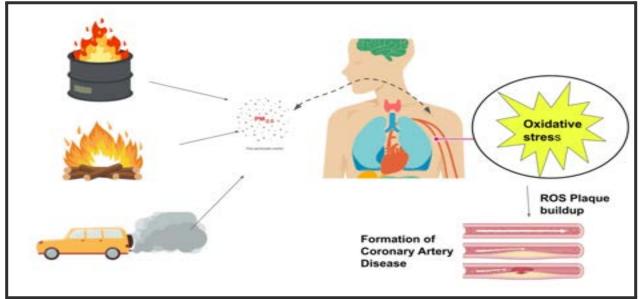
Characteristics of Fine Particulate Matter

Research has shown that particulate matter (PM) may be responsible for premature deaths caused by air pollution. Fine particulate matter is defined as particles that are 2.5 microns or fewer in diameter, typically described as tiny particles or droplets in the air. Examples include dust, dirt, smoke, and soot. PM2.5 particles come from various sources, including vehicle emissions, industrial processes, construction activities, and natural sources such as wildfires and dust storms. Naturally, particulate matter can be generated through volcanic eruptions and natural gaseous precursors. However, human activities frequently emit PM from construction sites, wildfires, wood burning, agricultural activities, dusty roads, car exhaust, and factory emissions. Due to their small size, PM2.5 particles can remain suspended in the air for long periods and travel long distances, affecting air quality locally, regionally, and globally. PM less than 10 micrometers in diameter poses the greatest risk to human health as it can penetrate the lungs and other vital organs easily.

General health risks of Fine Particulate Matter 2.5

The prevalence of PM2.5 poses a substantial risk primarily due to its adverse effects on the human body. Generally, exposure to unhealthy levels of PM2.5 can increase the risks of various health problems^[12]. For instance, PM2.5 can directly cause heart disease, asthma, and low birth weight. Additionally, individuals exposed to these particles may experience irregular heartbeat, nonfatal heart attacks, and decreased lung function. Moreover, PM2.5 can also result in vision impairments and a distorted sense of sight.





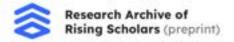
Connection between PM 2.5 and Reactive Oxygen Species (ROS)

Figure 3: Simple Diagram depicting the biological processes related to the formation of Coronary Artery Disease through PM exposure. Created by Sharath Jyothi.

Reactive Oxygen Species (ROS) are identified as offshoots of various metabolic reactions that occur in the body^[13]. More specifically, ROS can be categorized as highly reactive chemicals derived from diatomic oxygen. The three commonly known species are superoxide anion (O2-–), hydrogen peroxide (H2O2), and the hydroxyl radical (HO-), also known as "free radicals^[13]." ROS are important for the metabolism of oxygen and play a role in cell signaling pathways and homeostasis. Additionally, ROS can react with organic substrates, leading to intermediate species that can continue producing further ROS. However, research has shown that continuous ROS production can be detrimental to the body. Numerous studies involving the relationship between PM2.5 and ROS have indicated that PM2.5 exposure could increase ROS levels by disrupting cellular redox signaling or upregulating endogenous ROS production, thereby resulting in oxidative stress^[13]. Oxidative stress involves an imbalance of these species, which can consequently result in severe cell and tissue damage and even cardiovascular obstruction^[14].

Effects of PM 2.5 and ROS on Coronary Artery Disease formation

The underlying processes for many cardiovascular-related diseases related to particulate matter directly involve fine particles in the air translocating to circulatory/air pathways and indirect injury by inducing systemic inflammation^[15] and oxidative stress in circulation, consequently leading to cardiovascular damage and plaque buildup^{[16][17]}. Systemic oxidative stress induced by PM 2.5 exposure has also been closely linked with deficits in vascular compliance and flow-mediated dilation and an increase in arterial stiffness, consequently leading to premature endothelial cell death^[18]. Moreover, this is particularly dangerous for children due their prolonged exposure and shortened length of airways. As of 2022, exposure to PM 2.5 has even been associated with



reduced carotid artery distensibility in children under 5^[19]. Thus, it is imperative that PM 2.5 is addressed as a potential risk factor for the high rates of coronary artery disease in the south asian subcontinent.

Common Risk Factors of Coronary Artery Disease

The most common risk factors associated with CAD onset include high LDL (Low-Density Lipoprotein) cholesterol, low HDL (High-Density Lipoprotein) cholesterol, high blood pressure, family history, diabetes, smoking, and obesity^[20]. The progression of age is also closely related to the onset of CAD due to the physiological changes in the arteries with age. Moreover, men are genetically more at risk than women for CAD. These commonly known risk factors are vital for early detection and prediction; however, other risk factors, such as air pollution, especially in highly populated areas, need to be considered when addressing public health concerns.

The effects of Fine Particulate Matter on Coronary Artery Disease Rates in South Asia

Although the high rates of coronary artery disease (CAD) in South Asia can be attributed to reasons such as genetic differences, the relationship between highly polluted cities and the prevalence of CAD is statistically significant in many ways. In fact, a recent study^[21] conducted by Anand Krishnan and others measuring the fluctuations of CAD in rural and urban areas of New Delhi found significantly higher levels of CAD in urban areas than in rural areas. From 2010 to 2020, New Delhi experienced incredibly high PM2.5 levels and was also a global leader in cardiovascular disease, pointing to the possibility of micro air pollutants as an important risk factor for the development of CAD. As shown by the data below, a p-value of less than 0.001 was statistically significant and indicated that urban development had an effect on CAD development in females.

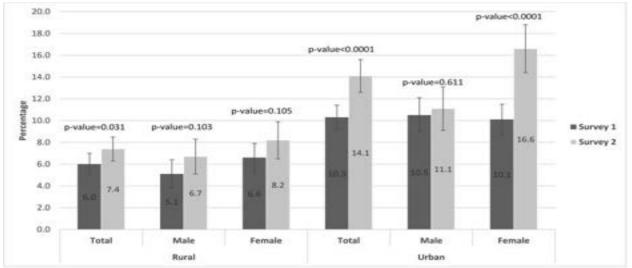
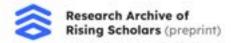


Figure 4: Diagram representing standardized CAD prevalence relative to ages/gender in New Delhi: Created by Anand Krishnan^[21].

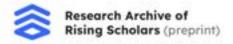


Although high CAD levels can also be attributed to genetic and socio-economic factors, the high levels of particulate matter in urban populated cities provide valuable insight into the role of pollution in the development of CAD, especially in industrialized regions. PM 2.5 is considerably higher in urban areas, pointing to the significance in understanding the impact of particle-level pollution on human health. In comparison to other factors, the level of pollution in this region is a vital marker for the progressive cardiovascular issues plaguing the nation over the same years.

A cross-sectional study over the duration of a year at a tertiary health care center in North India conducted in 2023 also investigated CAD prevalence in males and females^[22]. Similar to the previous study, the significance of this study lies in the fact that urban areas exhibited a substantially higher rate of coronary artery disease prevalence compared to rural areas. Additionally, urban residents displayed a higher count of risk factors, including hypertension, hyperlipidemia, diabetes mellitus, obesity, and ischemic heart disease, than rural residents. However, we do believe that the methodologies of this study may not be completely representative of the entire population due to the lack of random sampling. Along with this, the structured questionnaire that was used to determine the most prevalent risk factors does not take into account various confounding variables that may be of interest in the formation of CAD such as concentrations of particle-level pollution or even psychosocial issues. Despite this, we believe that the heightened amounts of air pollution in these areas play a large factor into the prevalence of increased risk factors, especially considering the already predisposed cardiovascular issues in South Asia^[23].

To gain more insight into this nuanced topic, we interviewed Lin Tan, a graduate student at the University of California Riverside. Tan's current research focuses on air pollution and aerosol-related topics in Asia. When responding to our pressing question, "Is particulate matter a deciding factor in the high rates of coronary artery disease or cardiovascular disease in South Asia?" Tan states, "The PM would likely increase the rate on top of any coronary artery or cardiovascular preconditions that already exist in the population. The PM may be a triggering factor of the diseases if the population already has other chronic problems. The economy of South Asia has been quickly growing. The PM levels in South Asia due to industrial growth and the use of coal in power plants are known to have grown significantly. But starting from 2018, the PM levels started to show a decreasing trend, which might be largely contributed by the COVID pandemic." Further expanding on the conclusion, he states, "But academically, while we agree that the PM is one of the factors that contribute to the increase of coronary disease in South Asia, we may not be able to conclude PM as the deciding factor because the coronary artery or cardiovascular preconditions of the population in South Asia may also be related to other leading factors like eating culture and lifestyle."

As more research is done on these interconnected topics, it is important to remember that the bulk concentration of PM does not tell the full story because PM is made of a variety of components and some even more harmful chemicals (e.g., polycyclic aromatic hydrocarbons). The sum effect of these PMs is related to their chemical composition and size/morphology properties, including oxidative stress potential, solubility, charge, surface area, particle count, lung deposition, and stability within the atmosphere and biological tissues. For example, particulate matter with transition metals, organic compounds, semiquinones, and endotoxin is shown to be highly relevant to cardiovascular diseases. Thus, it is important to look into the



regional composition of the PM if we want to further understand how PM pollution affects coronary artery disease or cardiovascular disease.

Ultimately, the harsh reality is that as the COVID-19 pandemic further dwindles down, particle level pollution will only get progressively worse in these areas. In fact as of late 2023, many doctors from India say there is a direct link between air pollution, pulmonary disease, worsened asthma, and impaired lung function^[23]. Pulmonologist Dr. Sourabh Pahuja, in particular, stated that he received a significant 40 to 50 percent increase in patients suffering from breathing related disorders such as ROPD^[24]. South Asians, being increasingly susceptible and predisposed to asthma related conditions, are increasingly prone to CAD formation as well^[25]. Although asthma is a lung condition, it serves as a serious risk factor for CAD development due to the chronic inflammation of the respiratory airways that it is characterized by. In addition, persistent pulmonary inflammation can lead to systemic inflammation, negatively stressing blood vessels and potentially triggering CAD development^[26].

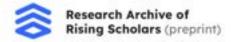
Effects of Other Pollutants (VOCs and Methane) on Coronary Artery Disease formation

Volatile Organic Compounds (VOCs) represent a diverse group of chemicals emanating from various sources, including vehicle emissions, industrial operations, everyday household items, and the burning of fuels. VOCs are significant contributors to air pollution and are linked with an increased risk of cardiovascular diseases such as Coronary Artery Disease (CAD). When VOCs are inhaled and enter the bloodstream, they induce systemic inflammation along with oxidative stress. These biological responses are vital in the development of atherosclerosis.

As inflammation escalates, biological markers including C-reactive protein (CRP) and interleukin-6 (IL-6) intensify plaque formation. Moreover, VOCs compromise endothelial function—a layer of cells lining the blood vessels—by limiting the availability of nitric oxide. This reduction leads to vasoconstriction and promotes further plaque buildup, thus elevating CAD risk.

Methane (CH4), significantly produced through agricultural methods, fossil fuel extraction, and waste management, also possesses indirect consequences on cardiovascular health. Although methane itself doesn't pose direct harm at typical ambient concentrations, it greatly aids in creating ground-level ozone via chemical reactions with other pollutants like nitrogen oxides (NOx) and VOCs. Known for its respiratory irritation capabilities, ground-level ozone similarly triggers systemic inflammation, oxidative stress, and endothelial dysfunction—paralleling the harmful effects of VOCs on cardiovascular wellness^[27].

The situation appears particularly dire in South Asia due to rampant urbanization, dense populations, and comprehensive industrial activities that magnify emissions of these pollutants. In this region's urban settings—metropolises like New Delhi witness higher concentrations of VOCs and methane than rural areas—such factors culminate in increased CAD prevalence ^{28]}. Tackling this issue effectively demands strict regulatory actions aimed at curbing emissions. This includes mitigating vehicle emissions, advocating for cleaner industrial processes, and refining agricultural practices. Implementing these robust air quality management strategies is



imperative for safeguarding public health and diminishing the prevalence of cardiovascular diseases across South Asia.

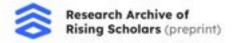
Conclusion

This study scrutinized the correlation between air pollutants and Coronary Artery Disease (CAD) in South Asia, focusing on fine particulate matter (PM2.5), Volatile Organic Compounds (VOCs), and methane. These pollutants contribute to CAD development through oxidative stress and inflammation. The rapid urbanization and industrialization in South Asia have exacerbated air pollution, posing a significant risk to millions. Addressing this issue necessitates comprehensive strategies to decrease emissions, promote cleaner energy, and enforce air quality standards. Combating air pollution presents a crucial public health challenge, requiring robust policies and international collaboration to enhance air quality and reduce CAD prevalence in South Asia and beyond.

We do also acknowledge the fact that pollution has gradually gotten better in these highly polluted areas, especially after the COVID-19 pandemic. However, we still highlight the unusual connection to which the most polluted regions globally, being nations in the South Asian subcontinent, are also leaders in cardiovascular disease and CAD development.

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References

1. Gangwar, R. S., Bevan, G. H., Palanivel, R., Das, L., & Rajagopalan, S. (2020). Oxidative stress pathways of air pollution mediated toxicity: Recent insights. *Redox Biology*, *34*, 101545. https://doi.org/10.1016/j.redox.2020.101545

2. Samad, Z., & Hanif, B. (2023). Cardiovascular diseases in Pakistan: Imagining a postpandemic, postconflict future. *Circulation*, *147*(17), 1261–1263. https://doi.org/10.1161/circulationaha.122.059122

3. Thangavel, P., Park, D., & Lee, Y. (2022). Recent Insights into Particulate Matter (PM2.5)-Mediated Toxicity in Humans: An Overview. *International Journal of Environmental Research and Public Health*, *19*(12), 7511. https://doi.org/10.3390/ijerph19127511

4. Vanzo, T. (2024, June 27). Top 25 Cities with Worst Air Pollution (2024 Rankings). Smart Air. https://smartairfilters.com/en/blog/top-cities-worst-air-pollution/

5. AQI Basics | AirNow.gov. (n.d.). https://www.airnow.gov/aqi/aqi-basics

6. *Particulate Matter (PM) Basics* | *US EPA*. (2024, June 20). US EPA. https://www.epa.gov/pm-pollution/particulate-matter-pm-basics

7. Guttikunda, S., & Ka, N. (2022). Evolution of India's PM2.5 pollution between 1998 and 2020 using global reanalysis fields coupled with satellite observations and fuel consumption patterns. *Environmental Science Atmospheres*, *2*(6), 1502–1515. https://doi.org/10.1039/d2ea00027j

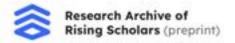
8. India Today. (2023, October 29). *Air pollution is killing you, slowly*| *Health360*| *Sneha Mordani* [Video]. YouTube. https://www.youtube.com/watch?v=MHZD3NCaeEk

9. Swarnakar, R., & Dhar, R. (2024). Call to action: Addressing asthma diagnosis and treatment gaps in India. *Lung India*, *41*(3), 209–216. https://doi.org/10.4103/lungindia.lungindia_518_23

10. *Conditions treated*. (n.d.). Stanford Health Care. https://stanfordhealthcare.org/medical-clinics/stanford-south-asian-translational-heart-initiative/c onditions.html#:~:text=Coronary%20artery%20disease%20in%20South,of%20the%20

11. Krishnan, A., Asadullah, M., Roy, A., Praveen, P. A., Singh, K., Amarchand, R., Gupta, R., Ramakrishnan, L., Kondal, D., Tandon, N., Sharma, M., Shukla, D. K., Prabhakaran, D., & Reddy, K. S. (2020). Change in prevalence of Coronary Heart Disease and its risk between 1991-94 to 2010-12 among rural and urban population of National Capital Region, Delhi. *Indian Heart Journal*, *72*(5), 403–409. https://doi.org/10.1016/j.ihj.2020.08.008

12. *Health and Environmental Effects of Particulate matter (PM)* | *US EPA*. (2024, July 16). US EPA. https://www.epa.gov/pm-pollution/health-and-environmental-effects-particulate-matter-pm



13. Collin, F. (2019). Chemical basis of reactive oxygen species reactivity and involvement in neurodegenerative diseases. *International Journal of Molecular Sciences*, *20*(10), 2407. https://doi.org/10.3390/ijms20102407

14. Garcia, A., Santa-Helena, E., De Falco, A., De Paula Ribeiro, J., Gioda, A., & Gioda, C. R. (2023). Toxicological Effects of Fine Particulate Matter (PM2.5): Health Risks and Associated Systemic Injuries—Systematic Review. *Water Air & Soil Pollution*, *234*(6). https://doi.org/10.1007/s11270-023-06278-9

15. Bhatnagar, A. (2022). Cardiovascular effects of particulate air pollution. *Annual Review of Medicine*, 73(1), 393–406. https://doi.org/10.1146/annurev-med-042220-011549

16. Collin, F. (2019). Chemical basis of reactive oxygen species reactivity and involvement in neurodegenerative diseases. *International Journal of Molecular Sciences*, *20*(10), 2407. https://doi.org/10.3390/ijms20102407

17. Basith, S., Manavalan, B., Shin, T. H., Park, C. B., Lee, W., Kim, J., & Lee, G. (2022). The impact of fine particulate Matter 2.5 on the cardiovascular system: A review of the Invisible Killer. *Nanomaterials*, *12*(15), 2656. https://doi.org/10.3390/nano12152656

18. Garcia, A., Santa-Helena, E., De Falco, A., De Paula Ribeiro, J., Gioda, A., & Gioda, C. R. (2023). Toxicological Effects of Fine Particulate Matter (PM2.5): Health Risks and Associated Systemic Injuries—Systematic Review. *Water Air & Soil Pollution*, *234*(6). https://doi.org/10.1007/s11270-023-06278-9

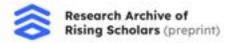
19. Bhatnagar, A. (2022). Cardiovascular effects of particulate air pollution. *Annual Review of Medicine*, 73(1), 393–406. https://doi.org/10.1146/annurev-med-042220-011549

20. Shahjehan, R. D., & Bhutta, B. S. (2023, August 17). *Coronary artery disease*. StatPearls - NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK564304/

21. Krishnan, A., Asadullah, M., Roy, A., Praveen, P. A., Singh, K., Amarchand, R., Gupta, R., Ramakrishnan, L., Kondal, D., Tandon, N., Sharma, M., Shukla, D. K., Prabhakaran, D., & Reddy, K. S. (2020). Change in prevalence of Coronary Heart Disease and its risk between 1991-94 to 2010-12 among rural and urban population of National Capital Region, Delhi. *Indian Heart Journal*, *72*(5), 403–409. https://doi.org/10.1016/j.ihj.2020.08.008

22. Akhtar, N., Paul, P., Kumar, T., & Paul, U. K. (2023). Prevalence of coronary artery disease and the associated risk factors among the patients attending the medicine department in a tertiary care teaching hospital in the North Eastern Zone in India. *International Journal of Advances in Medicine*, *10*(12), 823–829. https://doi.org/10.18203/2349-3933.ijam20233565

23. Cover Story | South Asians and Cardiovascular Disease: The Hidden Threat - American College of Cardiology. (2019, May 7). American College of Cardiology. https://www.acc.org/latest-in-cardiology/articles/2019/05/07/12/42/cover-story-south-asians-and-cardiovascular-disease-the-hidden-threat.



24. India Today. (2023, October 29). *Air pollution is killing you, slowly*| *Health360*| *Sneha Mordani* [Video]. YouTube. https://www.youtube.com/watch?v=MHZD3NCaeEk

25. Chen, E. (2024, February 12). Stem cell study offers clue to South Asians' increased risk of cardiovascular disease. *STAT*.

https://www.statnews.com/2024/02/12/south-asians-cardiovascular-disease-stem-cells/#:~:text= Stem%20cell%20study%20offers%20clue,increased%20risk%20of%20cardiovascular%20disea se&text=A%20growing%20body%20of%20data,clear%20what%20explains%20this%20disparity

26. Garg, V. S., Sojitra, M. H., Ubhadiya, T. J., Dubey, N., Shah, K., Gandhi, S. K., & Patel, P. (2023). Understanding the link between adult asthma and coronary artery Disease: A Narrative review. *Cureus*. https://doi.org/10.7759/cureus.43621

27. Effects of methane in cardiovascular system | Kedvesné dr. Kupai Krisztina: Emergent role of antioxidant enzymes and gasotransmitters in the myocardium. (n.d.). http://www.jgypk.hu/tamop15e/tananyag_html/myocardium/effects_of_methane_in_cardiovascul ar_system.html

28. Jain, V., Tripathi, N., Tripathi, S. N., Gupta, M., Sahu, L. K., Murari, V., Gaddamidi, S., Shukla, A. K., & Prevot, A. S. H. (2023). Real-time measurements of non-methane volatile organic compounds in the central Indo-Gangetic basin, Lucknow, India: source characterisation and their role in O3 and secondary organic aerosol formation. *Atmospheric Chemistry and Physics*, *23*(5), 3383–3408. https://doi.org/10.5194/acp-23-3383-2023