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Relation between Anthropogenic Air Pollution and Diabetes Mellitus.

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Abstract

Diabetes mellitus has emerged as one of the most pressing global health challenges, with both genetic predisposition and environmental triggers contributing to its prevalence. While lifestyle factors such as diet, obesity, and physical inactivity are well-documented, the role of anthropogenic air pollution in diabetes onset and progression has gained considerable scientific attention in recent years. Airborne pollutants such as particulate matter (PM2.5 and PM10), sulphur dioxide (SO_2), nitrogen dioxide (NO_2), ozone (O_3), aerosols, smoke, and excess carbon dioxide (CO_2) not only impair respiratory and cardiovascular systems but also play a critical role in systemic inflammation, oxidative stress, and insulin resistance, all of which are key mechanisms linked to the development of type 2 diabetes. This paper seeks to synthesize the current understanding of how these pollutants contribute to diabetes risk and highlight the public health implications of this emerging association.

Keywords

Signalling, insulin resistance, inflammation, particulate matters, health

Introduction

Air pollution, particularly from anthropogenic sources, is one of the leading environmental threats of the 21st century. Epidemiological and experimental studies demonstrate that exposure to ambient air pollutants is closely associated with the development of metabolic disorders, especially type 2 diabetes (Brook et al., 2010; Rao et al., 2015). Among these pollutants, fine particulate matter (PM2.5) has been shown to penetrate deep into the alveoli, translocate into systemic circulation, and trigger chronic low-grade inflammation and endothelial dysfunction, both of which exacerbate insulin resistance (Rajagopalan et al., 2018; Liu et al., 2019). Similarly, PM10 exposure is associated with impaired glucose tolerance and heightened oxidative stress, further linking coarse particles to diabetes pathophysiology (Balti et al., 2014).

Gaseous pollutants also play a significant role. Sulphur dioxide (SO_2) and nitrogen dioxide (NO_2), primarily released from fossil fuel combustion and industrial processes, promote systemic oxidative stress and vascular inflammation, contributing to impaired glucose metabolism (Wang et al., 2014; Liu et al., 2016). Ozone (O_3), a secondary pollutant formed through photochemical reactions, has been linked to β-cell dysfunction and aggravated insulin resistance through its pro-oxidant properties (Coogan et al., 2016).

Other airborne contaminants such as aerosols and smoke amplify these effects by increasing oxidative burden and impairing endothelial nitric oxide signalling, thereby worsening metabolic dysregulation (Fang et al., 2014). Moreover, chronic exposure to elevated atmospheric carbon dioxide (CO_2) not only contributes to climate change

but also indirectly influences diabetes prevalence by exacerbating oxidative stress and systemic inflammation in susceptible populations (Rao et al., 2015).

Collectively, these pollutants create a metabolic environment conducive to diabetes development by interacting with key molecular pathways, including Akt signalling, endothelial nitric oxide synthase phosphorylation, and inflammatory cytokine up regulation (Brook et al., 2010; Rajagopalan et al., 2018). Understanding these associations is critical for public health policy, as mitigating air pollution may serve as a complementary strategy to reduce the global diabetes burden.

This study illustrates the interrelationships between the 8 kinds of air pollutants with that of Diabetes mellitus.

1. $PM_{2.5}$, relation to Akt Pathway Disruption, and Insulin Resistance

The phosphoinositide 3-kinase (PI3K)/Akt pathway plays a central role in insulin signalling by promoting glucose uptake, glycogen synthesis, and lipid metabolism. Activation of Akt is crucial for translocation of glucose transporter-4 (GLUT4) to the plasma membrane in skeletal muscle and adipose tissue, as well as suppression of gluconeogenesis in the liver (Saltiel & Kahn, 2001). Chronic exposure to fine particulate matter ($PM_{2.5}$) has been implicated in disrupting this pathway, thereby promoting insulin resistance and the development of type 2 diabetes mellitus (T2DM).

Experimental and epidemiological studies demonstrate that $PM_{2.5}$ increases systemic oxidative stress and inflammation, leading to impaired insulin signalling. In murine models, sub acute $PM_{2.5}$ exposure elevated hepatic and skeletal muscle levels of reactive oxygen species (ROS), TNF-α, and IL-6, while significantly reducing phosphorylation of PI3K and Akt (Liu et al., 2019). This molecular impairment translated into impaired glucose tolerance and elevated homeostatic model assessment of insulin resistance (HOMA-IR), consistent with insulin resistance. Similarly, in adipose tissue, $PM_{2.5}$ exposure disrupted Akt phosphorylation and reduced GLUT4 expression, further aggravating glucose dysregulation (Sun et al., 2013). Mechanistically, inflammatory cytokines induced by $PM_{2.5}$ interfere with insulin receptor substrate-1 (IRS-1) activity, thereby attenuating downstream PI3K/Akt signalling (Brook et al., 2010).

These findings provide a mechanistic explanation for epidemiological observations linking long-term $PM_{2.5}$ exposure to increased incidence of insulin resistance and T2DM in humans. For example, cohort studies have associated higher ambient $PM_{2.5}$ exposure with elevated fasting glucose and HbA1c levels, suggesting that pollution-induced PI3K/Akt dysfunction contributes to metabolic disease risk (Rajagopalan & Brook, 2012). Collectively, evidence indicates that $PM_{2.5}$ exposure disrupts insulin signaling by impairing Akt phosphorylation via oxidative and inflammatory pathways, thereby playing a pivotal role in the pathogenesis of insulin resistance.

Endothelial nitric oxide synthase (eNOS) , P2.5 and insulin resistance

Endothelial nitric oxide synthase (eNOS) phosphorylation is a key regulator of endothelial function, and its dysregulation has been strongly linked to cardiometabolic disorders. Under physiological conditions, eNOS

becomes phosphorylated at specific serine residues (e.g., Ser1177), which enhances nitric oxide (NO) production. NO maintains vascular tone, insulin-stimulated glucose uptake, and anti-inflammatory signaling. However, exposure to fine particulate matter (PM2.5) from air pollution interferes with this pathway.

Experimental and epidemiological studies demonstrate that PM2.5 exposure induces oxidative stress and activates inflammatory signaling cascades, including NF-κB and JNK pathways. This leads to decreased eNOS phosphorylation at activating sites and increased phosphorylation at inhibitory sites (e.g., Thr495). As a result, bioavailable NO is reduced, and endothelial dysfunction occurs. Importantly, impaired NO signaling diminishes insulin-mediated vasodilation in skeletal muscle microvasculature, leading to reduced glucose uptake. Thus, disruption of eNOS phosphorylation in the endothelium constitutes a mechanistic link between PM2.5 exposure and the development of systemic insulin resistance.

Moreover, PM2.5 exposure enhances reactive oxygen species (ROS) generation and uncoupling of eNOS, shifting the enzyme from producing NO to superoxide. This not only exacerbates vascular oxidative stress but also further suppresses insulin receptor substrate (IRS)/PI3K/Akt signaling in endothelial cells, a critical axis for both vascular health and insulin sensitivity. Consequently, impaired eNOS phosphorylation due to air pollution contributes to a vicious cycle of endothelial dysfunction, inflammation, and metabolic dysregulation that predisposes to type 2 diabetes and cardiovascular disease.

2. PM_{10} and Diabetes

Particulate matter with an aerodynamic diameter ≤10 μm (PM_{10}) is a key component of ambient air pollution and has been increasingly associated with the development of type 2 diabetes. Inhaled PM_{10} particles deposit in the respiratory tract, where they generate reactive oxygen species (ROS) and activate inflammatory pathways, leading to systemic oxidative stress and chronic low-grade inflammation. These processes contribute to β-cell dysfunction and impaired insulin secretion, thereby promoting hyperglycemia (Eze et al., 2015; Peng et al., 2016).

In addition to inflammation, PM_{10} exposure is strongly linked to insulin resistance, largely through interference with insulin signalling pathways such as IRS-1 and Akt phosphorylation. Experimental and epidemiological studies indicate that chronic exposure reduces glucose uptake in muscle and adipose tissues, amplifying the metabolic disturbances associated with type 2 diabetes (Peng et al., 2016; Liu et al., 2019).

Another critical mechanism is endothelial dysfunction, since vascular endothelium regulates nitric oxide (NO) production and glucose transport. PM_{10} reduces NO bioavailability and promotes endothelial inflammation, which worsens glucose dysregulation and accelerates both microvascular and macrovascular diabetic complications (Liu et al., 2019).

Epidemiological evidence further supports these mechanistic links. Large cohort analyses in Europe and Asia demonstrate that for every 10 μg/m³ increase in PM_{10} exposure, the incidence of type 2 diabetes and related mortality significantly increases (Eze et al., 2015; Liu et al., 2019). Collectively, these findings highlight PM_{10} not only as a respiratory hazard but also as an environmental metabolic risk factor, contributing to

3. Carbon Dioxide (CO_2) and Diabetes

Although carbon dioxide (CO_2) is primarily regarded as a greenhouse gas contributing to global warming, its potential influence on metabolic health, including diabetes, has gained increasing attention. Elevated atmospheric CO_2 levels can indirectly affect diabetes risk through climate change–driven pathways such as heat stress, altered food quality, and reduced physical activity (Shen et al., 2021). Experimental studies suggest that chronic exposure to elevated CO_2 concentrations may impair insulin sensitivity by inducing low-grade systemic acidosis, oxidative stress, and mitochondrial dysfunction in target tissues (Lan et al., 2020). Moreover, prolonged CO_2 exposure has been associated with disturbances in pancreatic β-cell function, leading to dysregulated glucose homeostasis (Liu et al., 2019). Additionally, climate change fueled by rising CO_2 emissions exacerbates air pollution and promotes obesogenic environments, both of which are strong risk factors for type 2 diabetes (Hernandez et al., 2020). Thus, while CO_2 is not a classical air pollutant like particulate matter or ozone, its role as a driver of climate-mediated pathways places it as an indirect but significant contributor to the global diabetes burden.

4. Ozone and Diabetes

Ground-level ozone (O_3), a secondary air pollutant formed through photochemical reactions between nitrogen oxides (NO_x) and volatile organic compounds (VOCs) in the presence of sunlight, is increasingly recognized as an important contributor to non-communicable diseases beyond its established respiratory effects. Recent research suggests that ozone exposure is significantly associated with metabolic dysfunction and type 2 diabetes mellitus (T2DM).

Mechanistically, ozone inhalation triggers oxidative stress by generating excessive reactive oxygen species (ROS), overwhelming the antioxidant defense system. This process leads to impaired insulin signalling and reduced glucose uptake (Cai et al., 2016). In addition, ozone stimulates systemic inflammation through activation of NF-κB signalling and upregulation of pro-inflammatory cytokines such as IL-6, TNF-α, and CRP, which further exacerbate insulin resistance (Miller et al., 2016). Another important pathway is endothelial dysfunction, as ozone reduces the bioavailability of nitric oxide (NO) and alters vascular homeostasis, thereby impairing glucose transport to skeletal muscle and increasing diabetic vascular complications (Thompson et al., 2019). Ozone also contributes to adipose tissue dysfunction by modifying adipokine secretion—decreasing adiponectin and increasing leptin levels—thereby intensifying insulin resistance. Furthermore, long-term ozone exposure may damage pancreatic β-cells through mitochondrial dysfunction and epigenetic alterations, leading to reduced insulin secretion (Ren et al., 2019).

Epidemiological studies reinforce these mechanistic insights. A systematic review and meta-analysis reported that long-term ozone exposure was associated with increased risk of diabetes incidence and related complications (Cai et al., 2016). In a large-scale U.S. cohort study, chronic ozone exposure was significantly correlated with higher diabetes-related mortality (Thompson et al., 2019). Similarly, a nationwide cohort study

in China demonstrated that individuals living in areas with elevated ozone concentrations had increased fasting glucose and HbA1c levels, indicating impaired glycemic control (Ren et al., 2019). Collectively, these findings establish ozone as an under recognized environmental determinant of diabetes.

In summary, ozone exposure contributes to both the onset and progression of diabetes via multiple interlinked pathways, including oxidative stress, systemic inflammation, vascular dysfunction, adipose tissue dysregulation, and pancreatic β-cell impairment. These findings highlight the importance of addressing ozone pollution in the broader context of diabetes prevention and public health policy.

5. Nitrogen Oxides (NOx) and Diabetes

Nitrogen oxides (NO and NO_2), primarily emitted from vehicular exhaust, industrial combustion, and power plants, are major gaseous pollutants strongly linked to cardio metabolic diseases, including type 2 diabetes mellitus (T2DM). Inhalation of NOx leads to the generation of reactive oxygen species (ROS) and nitrosative stress, which induce systemic oxidative damage and activate inflammatory pathways (Brook et al., 2013). This chronic inflammation impairs insulin receptor signalling through serine phosphorylation of IRS-1 and reduced activation of the PI3K/Akt pathway, leading to insulin resistance in skeletal muscle and adipose tissue (Liu et al., 2019).

NO_2 also contributes to endothelial dysfunction by reducing nitric oxide (NO) bioavailability, impairing vasodilation, and decreasing glucose uptake in peripheral tissues (Rajagopalan et al., 2018). Moreover, NOx exposure enhances adipose tissue inflammation by increasing infiltration of pro-inflammatory macrophages and disrupting adipokine secretion (↓ adiponectin, ↑ leptin and resistin), thereby aggravating obesity-associated diabetes risk (Sun et al., 2017).

At the pancreatic level, nitrosative stress damages β-cell mitochondria, reducing insulin secretion and worsening hyperglycemia (Xu et al., 2011). Epidemiological studies consistently show that long-term NOx exposure is associated with higher fasting glucose, HbA1c, and increased incidence of T2DM, particularly in urban populations exposed to traffic-related air pollution (Andersen et al., 2012; Liu et al., 2019).

Collectively, NOx pollutants promote diabetes pathogenesis through oxidative and nitrosative stress, inflammation, endothelial dysfunction, adipose tissue dysregulation, and β-cell impairment, highlighting them as key contributors to the rising burden of metabolic diseases in polluted environments.

6. SO_2 and Its Effect on Diabetes

Sulphur dioxide (SO_2), a major anthropogenic air pollutant released from fossil fuel combustion, industrial activities, and vehicular emissions, has been increasingly associated with metabolic disorders including type 2 diabetes mellitus (T2DM). Upon inhalation, SO_2 and its derivatives generate excessive reactive oxygen species (ROS), triggering systemic oxidative stress and chronic low-grade inflammation, both of which are central mechanisms in the pathogenesis of insulin resistance (Brook et al., 2013). Experimental studies suggest that SO_2 exposure reduces endothelial nitric oxide (NO) bioavailability, impairing vascular function and glucose uptake,

thereby contributing to endothelial dysfunction frequently observed in diabetes (Rajagopalan et al., 2018). Furthermore, SO_2 alters adipose tissue homeostasis by promoting a pro-inflammatory macrophage phenotype and disrupting adipokine secretion, which exacerbates obesity-associated insulin resistance (Sun et al., 2017). Mitochondrial dysfunction in pancreatic β-cells induced by oxidative stress further diminishes insulin secretion capacity, aggravating hyperglycemia and disease progression (Xu et al., 2011). Epidemiological evidence supports these mechanistic findings, with cohort and cross-sectional studies showing positive associations between ambient SO_2 exposure and increased incidence of diabetes, elevated fasting glucose, and glycated hemoglobin (HbA1c) levels in exposed populations (Liu et al., 2019). Collectively, these findings highlight that SO_2 contributes to diabetes development through a combination of oxidative stress, endothelial dysfunction, adipose tissue inflammation, and β-cell impairment, underscoring the importance of air quality interventions in mitigating diabetes burden.

7. Smoke and Diabetes

7.1 Oxidative Stress and Inflammation

Smoke exposure, whether from cigarettes or biomass fuels, generates abundant reactive oxygen species (ROS) and free radicals, leading to oxidative stress and systemic inflammation. Pancreatic β-cells are particularly vulnerable due to their low antioxidant defenses, resulting in impaired insulin secretion and progressive glucose intolerance (Chowdhury et al., 2020; Rani et al., 2020). Chronic inflammation further exacerbates tissue injury and contributes to the development of type 2 diabetes.

7.2 Insulin Resistance

Nicotine and other toxic components of smoke activate inflammatory signalling cascades, which increase phosphorylation of insulin receptor substrate-1 (IRS-1), thereby reducing insulin sensitivity. This mechanism, combined with elevated circulating free fatty acids, directly contributes to insulin resistance, a hallmark of type 2 diabetes (Chang et al., 2023; Rani et al., 2020). Experimental studies demonstrate that chronic smoke exposure impairs glucose uptake in peripheral tissues, reinforcing its diabetogenic effect.

7.3 Endothelial Dysfunction

Endothelial health is critical for maintaining vascular tone and glucose homeostasis. Smoke exposure reduces nitric oxide bioavailability and induces vascular inflammation, resulting in endothelial dysfunction, which worsens both insulin resistance and diabetic complications (World Health Organization, 2025; Sinha et al., 2016). Elevated biomarkers of endothelial injury, such as soluble ICAM-1 and VCAM-1, are consistently reported in populations chronically exposed to biomass or tobacco smoke.

7.4 Adipose Tissue Dysfunction and Second-Hand Smoke

Adipose tissue serves as an endocrine organ regulating insulin sensitivity. Smoke exposure decreases adiponectin, a hormone that enhances insulin action, while increasing pro-inflammatory cytokines such as TNF-α and IL-6. This imbalance leads to adipose tissue dysfunction, further promoting insulin resistance (Vardavas et al., 2018;

Chang et al., 2023). Importantly, even second-hand and third-hand smoke exposures elevate diabetes risk. Meta-analyses show that non-smokers exposed to second-hand smoke have a 27–28% higher risk of type 2 diabetes (Sun et al., 2013; Li et al., 2023). Experimental studies in animal models additionally suggest that third-hand smoke induces oxidative stress and insulin resistance, highlighting its long-term diabetogenic potential (Martins-Green et al., 2025).

8. Aerosols and Diabetes

A growing body of evidence has identified aerosols, particularly fine particulate matter ($PM_{2.5}$ and ultrafine particles), as an important environmental determinant of metabolic dysfunction, including type 2 diabetes mellitus (T2DM). Aerosols are capable of penetrating the alveolar barrier and entering systemic circulation, where they exert widespread effects beyond the respiratory system. Several mechanistic pathways have been proposed to explain this association.

Firstly, aerosols induce oxidative stress and systemic inflammation, primarily through excessive reactive oxygen species (ROS) production and activation of pro-inflammatory cytokines such as TNF-α and IL-6. These cytokines interfere with insulin receptor signalling, contributing to insulin resistance (Rajagopalan & Brook, 2018). Secondly, aerosols impair endothelial function by reducing nitric oxide bioavailability via inhibition of endothelial nitric oxide synthase (eNOS), thereby exacerbating vascular dysfunction, a hallmark of diabetes and its complications (Brook et al., 2018).

Furthermore, aerosol exposure is linked to adipose tissue dysfunction, where changes in adipokine secretion (reduced adiponectin, increased leptin) promote insulin resistance and glucose intolerance (Liu et al., 2019). Chronic exposure also induces epigenetic modifications and mitochondrial damage in pancreatic β-cells, impairing insulin secretion and accelerating diabetes progression (Eze et al., 2015).

Epidemiological studies strongly support these mechanistic insights. Large-scale cohorts in Europe and North America have consistently demonstrated an increased risk of diabetes incidence among populations exposed to elevated levels of $PM_{2.5}$ (Eze et al., 2015). In South Asia, where aerosol concentrations remain among the highest globally due to biomass burning and vehicular emissions, the rising prevalence of diabetes has been closely correlated with urban air pollution (Rajagopalan & Brook, 2018).

Collectively, these findings suggest that aerosols contribute not only to the onset of diabetes but also to its progression through multiple interlinked pathways involving inflammation, oxidative stress, vascular dysfunction, and impaired β-cell function.

Conclusion

The relationship between anthropogenic air pollution and diabetes mellitus, particularly type 2 diabetes (T2DM), represents a growing frontier in environmental and metabolic health research. The evidence reviewed in this paper demonstrates that air pollutants—including particulate matter ($PM_{2.5}$ and PM_{10}), gaseous pollutants (NO_x, SO_2, O_3, CO_2), aerosols, and smoke—exert profound influences on glucose metabolism, insulin signalling, and vascular health. These interactions converge on common mechanistic pathways involving oxidative stress, systemic

inflammation, endothelial dysfunction, and pancreatic β-cell impairment, ultimately predisposing individuals to insulin resistance, hyperglycemia, and long-term diabetic complications.

1. Shared Mechanistic Pathways

Despite differences in chemical composition, source, and deposition patterns, nearly all pollutants examined share the ability to induce oxidative stress and chronic low-grade inflammation. Fine and ultrafine particulates ($PM_{2.5}$, aerosols, smoke-derived particles) penetrate deeply into the lungs and enter systemic circulation, where they generate reactive oxygen species (ROS). These reactive intermediates activate inflammatory pathways, such as NF-κB and JNK signalling, leading to increased secretion of pro-inflammatory cytokines including TNF-α, IL-6, and CRP. These cytokines interfere with insulin receptor substrate (IRS) activity and downstream PI3K/Akt signalling, a critical axis for glucose uptake in skeletal muscle and adipose tissue. Thus, pollutants converge on insulin resistance through disruption of fundamental molecular signalling pathways.

In addition, pollutants such as $PM_{2.5}$, PM_{10}, O_3, and NO_x impair endothelial nitric oxide synthase (eNOS) phosphorylation and reduce nitric oxide (NO) bioavailability. Since NO plays a dual role in maintaining vascular tone and facilitating insulin-mediated glucose uptake in skeletal muscle microvasculature, endothelial dysfunction constitutes a central link between air pollution and diabetes risk. Endothelial injury not only worsens insulin resistance but also accelerates the vascular complications of diabetes, including nephropathy, neuropathy, and retinopathy.

2. Pollutant-Specific Mechanisms

While overlapping mechanisms are evident, pollutant-specific effects warrant attention.

$PM_{2.5}$ is strongly implicated in Akt pathway disruption, leading to reduced GLUT4 translocation and impaired glucose uptake. It also disrupts eNOS phosphorylation, creating a dual burden of metabolic and vascular dysfunction.

PM_{10} exerts diabetogenic effects through β-cell dysfunction in addition to systemic inflammation, highlighting its ability to impair both insulin secretion and action.

CO_2, though not a conventional pollutant, indirectly contributes to diabetes through climate-mediated pathways, including heat stress, food insecurity, and sedentary behaviors. Experimental evidence also links chronic CO_2 exposure to mitochondrial dysfunction and systemic acidosis, which impair insulin sensitivity.

O_3 is notable for its capacity to generate ROS directly and disrupt adipokine balance, lowering adiponectin and increasing leptin levels. This unique pathway emphasizes ozone's role in adipose tissue dysfunction, an underappreciated contributor to diabetes.

NO_x compounds introduce nitrosative stress, a distinct mechanism characterized by peroxynitrite formation and mitochondrial injury in β-cells, thereby reducing insulin secretion capacity.

SO_2 further exacerbates adipose tissue inflammation and alters macrophage phenotypes, promoting insulin resistance via immunometabolic pathways.

Smoke, particularly from cigarettes and biomass fuels, represents a complex mixture of particulates, heavy metals, and organic compounds. Beyond oxidative stress and inflammation, nicotine itself directly disrupts insulin receptor function, underscoring how lifestyle and environmental pollutants overlap in shaping diabetes risk.

Aerosols combine features of $PM_{2.5}$ and ultrafine particles, with their ability to cross the alveolar barrier and trigger systemic epigenetic changes. By altering gene expression patterns in β-cells and insulin-sensitive tissues, aerosols may promote long-term, transgenerational effects on metabolic health.

3. Epidemiological Evidence

The mechanistic findings are strongly supported by large-scale epidemiological studies. Cohorts in North America, Europe, and Asia consistently demonstrate positive associations between long-term exposure to $PM_{2.5}$, PM_{10}, NO_2, SO_2, and O_3 with increased incidence of T2DM, elevated fasting glucose, higher HbA1c levels, and greater diabetes-related mortality. Importantly, dose-response relationships have been documented, wherein each incremental rise in pollutant concentration corresponds to measurable increases in diabetes risk. For example, a 10 $\mu g/m^3$ increase in PM_{10} or $PM_{2.5}$ exposure significantly elevates the incidence of T2DM in multiple studies. These findings underscore the robustness of the association and suggest causality rather than mere correlation.

4. Public Health Implications

The convergence of mechanistic and epidemiological evidence establishes air pollution as a significant, yet under recognized, determinant of global diabetes burden. Unlike classical risk factors such as obesity, diet, and physical inactivity, air pollution represents an unavoidable exposure in many urban environments, disproportionately

affecting socioeconomically disadvantaged populations. This introduces an environmental justice dimension, wherein vulnerable communities bear a dual burden of pollution-related respiratory disease and metabolic disorders.

Furthermore, the interaction between air pollution and traditional risk factors may be synergistic rather than additive. For example, individuals with obesity or pre-existing insulin resistance may be more susceptible to pollution-induced metabolic injury, amplifying their risk of progression to overt diabetes. Similarly, pollution exposure during pregnancy may predispose offspring to metabolic dysfunction via epigenetic programming, raising concerns about intergenerational health effects.

5. Future Research Directions

Despite substantial progress, several gaps remain. First, the relative contributions of specific pollutants in complex urban mixtures are difficult to disentangle. Multi-pollutant models and advanced exposure assessments are needed to clarify these interactions. Second, most studies have focused on PM and O_3, while the roles of emerging pollutants such as ultrafine nanoparticles, volatile organic compounds (VOCs), and indoor air contaminants remain poorly defined. Third, mechanistic studies must integrate multi-omics approaches—including epigenomics, transcriptomics, and metabolomics—to capture the full spectrum of pollution-induced metabolic dysregulation.

Another key area is intervention research. While pharmacological agents targeting oxidative stress or inflammation may mitigate pollution-induced injury, structural interventions—such as cleaner fuels, stricter emission regulations, and urban green spaces—are likely to yield broader and more sustainable benefits. Understanding the cost-effectiveness of such interventions in reducing diabetes incidence could inform public health policies worldwide.

6. Conclusion and Call to Action

In conclusion, the body of evidence indicates that air pollution is not merely a respiratory hazard but a systemic threat with profound metabolic consequences. The pollutants reviewed—$PM_{2.5}$, PM_{10}, CO_2, O_3, NO_x, SO_2, smoke, and aerosols—contribute to diabetes pathogenesis through overlapping pathways of oxidative stress, inflammation, endothelial dysfunction, adipose tissue dysregulation, and β-cell impairment. These effects converge on critical nodes of insulin signalling, particularly the IRS/PI3K/Akt pathway, as well as endothelial nitric oxide signalling, creating a mechanistic basis for epidemiological associations with diabetes incidence and progression.

Given the global rise in both air pollution and diabetes prevalence, the intersection of these two public health crises demands urgent attention. Policies aimed at reducing air pollution may yield dual benefits: improving respiratory

and cardiovascular outcomes while simultaneously curbing the growing epidemic of diabetes. Clinicians should also recognize environmental exposures as part of comprehensive diabetes risk assessment, particularly in urban and industrialized regions.

Ultimately, addressing air pollution as a modifiable environmental determinant of diabetes requires a multidisciplinary approach that bridges molecular biology, epidemiology, urban planning, and policy. By framing diabetes prevention within the broader context of environmental health, we can move toward a more integrated and sustainable strategy for combating non-communicable diseases in the 21st century.

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