Journal of Social Research

P-ISSN:2827-9832
E-ISSN: 2828-335x
Vol. 5, No. 8, July 2026
http://ijsr.internationaljournallabs.com/index.php/ijsr

The Synergistic Effects of Lifestyle Factors and Air Pollution on Pancreatic Dysfunction and Metabolic Disorders: A Literature Review

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Keywords:
Pancreatic Dysfunction; PM2.5 Exposure; Unhealthy Lifestyle; Oxidative Stress.

ABSTRACT

Pancreatic dysfunction, particularly involving β-cell failure, is a central factor in the pathogenesis of metabolic disorders. Although intrinsic mechanisms of pancreatic damage have been extensively documented, the combined effects of behavioral and environmental stressors remain an important area of investigation. This literature review synthesized epidemiological and experimental evidence regarding the synergistic effects of lifestyle-related factors and ambient air pollution on pancreatic health. Unhealthy lifestyle behaviors, including obesity, high-fat dietary patterns, physical inactivity, cigarette smoking, and excessive alcohol consumption, contribute to metabolic impairment through glucolipotoxicity, redox imbalance, and systemic inflammation. These factors promote gut dysbiosis and disrupt key insulin signaling pathways. Concurrently, exposure to ambient air pollutants, particularly fine particulate matter ($PM_{2.5}$), may exacerbate these pathological processes. Particulate matter exposure induces oxidative stress, mitochondrial dysfunction, and endoplasmic reticulum (ER) stress, thereby activating the unfolded protein response (UPR) and NLRP3 inflammasome pathways. The convergence of adverse lifestyle behaviors and chronic air pollution exposure produces synergistic effects that accelerate β-cell apoptosis and disrupt metabolic homeostasis. Integrated preventive strategies addressing both behavioral modifications and environmental interventions are essential to reduce the increasing burden of type 2 diabetes mellitus in modern industrialized societies.

INTRODUCTION

Diabetes mellitus (DM) has emerged as a critical global health challenge, with a continuously increasing prevalence trend. According to the International Diabetes Federation (IDF) Diabetes Atlas 2025, approximately 11.1% of the global adult population, equivalent to 589 million individuals, are living with diabetes. In Indonesia, this burden is further intensified by rapid epidemiological transitions and urbanization, which significantly reshape population risk profiles (International Diabetes Federation, 2025). The increasing incidence of DM is no longer viewed solely as an individual clinical issue but rather as a systemic consequence of complex interactions among genetic predisposition, sedentary lifestyle patterns, and environmental degradation (Ong et al., 2023).

From a pathophysiological perspective, the progression of type 2 diabetes mellitus (T2DM) is primarily driven by chronic low-grade inflammation that disrupts the pancreatic islet microenvironment. This persistent inflammatory state is closely associated with metabolic stressors, including hyperglycemia, dyslipidemia, and elevated free fatty acid

levels, which activate innate immune responses within the islets of Langerhans. Pancreatic islet macrophages, as key regulators of this process, exhibit functional plasticity and undergo polarization toward a pro-inflammatory M1 phenotype through activation of Toll-like receptor 4 (TLR4) and the NLRP3 inflammasome pathways. This activation results in excessive production of pro-inflammatory cytokines, particularly interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α), which exert cytotoxic effects on pancreatic β-cells and impair insulin secretory function. In parallel, the inflammatory microenvironment is further aggravated by enzymatic mediators such as phospholipase A2 (PLA2) and proteases, including elastase, which contribute to membrane degradation, extracellular matrix remodeling, and disruption of islet structural integrity. The combined effects of cytokine-induced toxicity, oxidative stress, and enzymatic damage progressively reduce β-cell mass and function through apoptosis and functional impairment, ultimately resulting in decreased glucose-stimulated insulin secretion and systemic dysregulation of glycemic control, which are characteristic features of T2DM (Liu et al., 2020; Böni-Schnetzler & Meier, 2019; Alfadul et al., 2022; Zhang et al., 2021).

Although intrinsic mechanisms of β-cell damage have been extensively studied, the combined influence of external environmental and lifestyle-related factors requires further investigation. Fine particulate matter ($PM_{2.5}$), due to its small aerodynamic diameter, can bypass respiratory defense mechanisms, induce airway and pulmonary inflammation, and enter systemic circulation, thereby affecting multiple organs. Importantly, this systemic inflammatory response and oxidative stress contribute to metabolic dysregulation, positioning $PM_{2.5}$ as a significant environmental risk factor for the development and progression of T2DM, particularly among urban populations (Krittanawong et al., 2023). Concurrently, unhealthy lifestyle behaviors, including high-fat dietary patterns, physical inactivity, smoking, and excessive alcohol consumption, contribute to systemic oxidative stress and metabolic dysfunction (Szymkowicz et al., 2023). Evidence indicates that urban populations are frequently exposed to both environmental and lifestyle-related risk factors simultaneously, creating synergistic effects that accelerate pancreatic dysfunction through overlapping inflammatory pathways (Reyed, 2026).

The urgency of this research is highlighted by the accelerating global burden of diabetes and the widespread prevalence of lifestyle-related and environmental risk factors. With more than 589 million adults currently living with diabetes and projections indicating continued growth (International Diabetes Federation, 2025), identifying modifiable risk factors and their interactions is essential for developing effective prevention strategies. In many rapidly developing regions, urbanization is accompanied by dietary transitions toward high-fat, high-calorie foods and declining air quality, creating conditions that amplify diabetes risk through synergistic mechanisms (Liu et al., 2022). Understanding these interactions is crucial for developing targeted interventions that address the multifactorial nature of diabetes risk in modern environments.

To date, most studies have examined the effects of air pollution and lifestyle factors on metabolic disorders independently. A significant research gap remains in understanding how interactions between these factors operate at the molecular level to contribute to pancreatic dysfunction. This literature review aimed to synthesize current evidence regarding the interplay between environmental pollutants and lifestyle behaviors in relation to pancreatic

health. A comprehensive understanding of these mechanisms is essential for developing more effective preventive strategies, particularly for populations living in increasingly industrialized and urbanized environments.

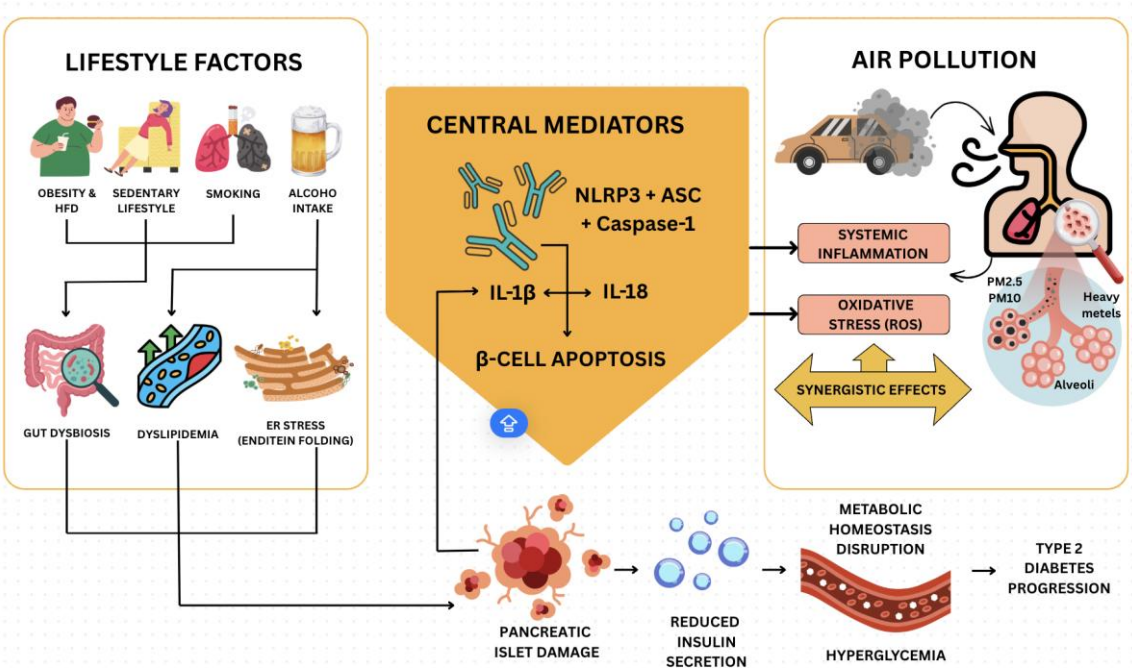

Figure 1. Lifestyle & Air Pollution: Modifiable Risk Factors for Pancreatic Dysfunction

METHOD

This literature review was conducted through a comprehensive search of scientific literature from electronic databases, including PubMed, Scopus, ScienceDirect, and Google Scholar, to identify studies examining the relationship between unhealthy lifestyle factors, air pollution exposure, and pancreatic dysfunction. The literature search was performed using combinations of keywords and Boolean operators (AND/OR), including "pancreatic dysfunction," "pancreatic damage," "β-cell dysfunction," "air pollution," "$PM_{2.5}$," "high-fat diet," "obesity," "smoking," "alcohol consumption," "sedentary behavior," "oxidative stress," "inflammation," "NLRP3 inflammasome," and "type 2 diabetes mellitus." Articles published in English between 2016 and 2026 were prioritized to obtain recent evidence, while highly relevant earlier studies were also included. The selected studies comprised experimental, observational, and review articles addressing pancreatic outcomes associated with environmental and lifestyle-related exposures. Titles, abstracts, and full texts were screened based on relevance, and the eligible studies were synthesized narratively to summarize the mechanisms linking these exposures to pancreatic impairment and metabolic dysfunction.

RESULTS AND DISCUSSION

Concept and Physiological Functions of the Pancreas

The pancreas is a heterocrine gland that performs both exocrine and endocrine functions, each playing a crucial role in metabolic homeostasis. Structurally, the endocrine portion accounts for approximately 2% of the total pancreatic mass, yet it plays a central role in blood glucose regulation through the islets of Langerhans. These islets are composed of five major

cell types, including α-cells that secrete glucagon, β-cells that produce insulin, δ-cells that secrete somatostatin, ε-cells that produce ghrelin, and pancreatic polypeptide (PP) cells that secrete pancreatic polypeptide. Among these, β-cells serve as the primary regulators of glucose homeostasis and constitute approximately 50–60% of the total islet cell mass, while α-cells account for 30–45%, and δ-cells and PP cells each comprise less than 10%, with ε-cells representing around 1%. To meet high metabolic demands, the islets of Langerhans are supported by a dense microvascular network, resulting in a blood supply more than fivefold greater than that of the surrounding exocrine tissue. This extensive vascularization facilitates efficient nutrient sensing and rapid hormone secretion; however, it may also increase the islets' vulnerability to circulating toxins and inflammatory mediators (Adams & Blum, 2022).

Mechanisms of Pancreatic Dysfunction : Inflammation and Oxidative Stress

Pancreatic dysfunction, particularly involving β-cells, arises from a complex interplay of systemic inflammation, oxidative stress, and metabolic imbalances. Pro-inflammatory cytokines such as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) interfere with insulin signaling by activating stress-related kinases, including c-Jun N-terminal kinase (JNK) and IκB kinase (IKK). These kinases promote inhibitory serine phosphorylation of insulin receptor substrate-1 (IRS-1), thereby attenuating insulin receptor signaling and downstream metabolic pathways. Consequently, glucose uptake especially in skeletal muscle is reduced due to impaired translocation of glucose transporter type 4 (GLUT4) to the plasma membrane (Liu et al., 2022).

Chronic exposure to inflammatory cytokines further suppresses insulin receptor autophosphorylation, reduces tyrosine phosphorylation of phosphatidylinositol 3-kinase (PI3K) associated proteins, and weakens Akt activation, thereby aggravating insulin resistance (Sun et al., 2022). Oxidative stress, driven by excessive production of reactive oxygen species (ROS), is a major contributor to β-cell damage during T2DM development. Elevated ROS directly impair insulin synthesis and secretion, while chronic inflammation, particularly in adipose tissue, alters adipokine profiles and promotes systemic insulin resistance (Molehin et al., 2020).

Pancreatic islets are especially vulnerable to oxidative injury due to their inherently low expression of antioxidant enzymes, rendering β-cells highly susceptible to dysfunction. Beyond β-cell impairment, ROS contribute to diabetic complications such as nephropathy, neuropathy, and retinopathy through lipid, protein, and DNA damage and persistent activating of NF-κB-mediated inflammatory pathways **(Brownlee, 2005; Nenna et al., 2020; Rohm et al., 2022)**.

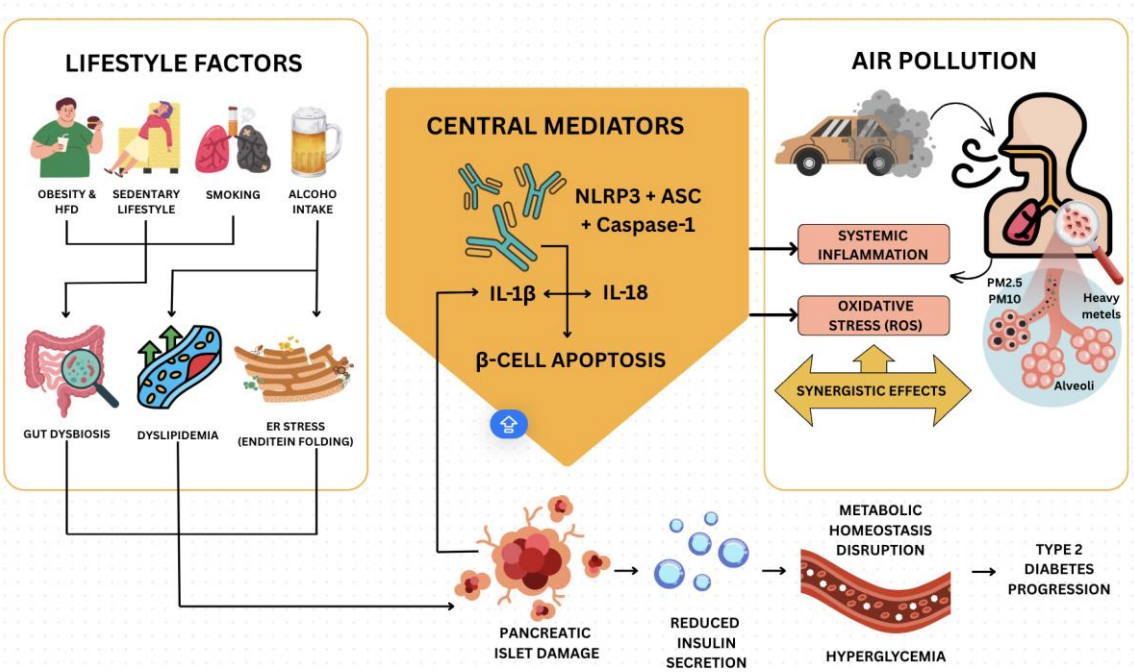

Figure 1. Schematic illustration summarizing mechanisms identified from the reviewed literature

Pathophysiological Impact of Lifestyle Factors on Pancreas

1. Obesity and Hight-fat diet (HFD)

A high-fat diet (HFD) is a major contributing factor to obesity and is closely associated with chronic low-grade inflammation, characterized by hypertrophic visceral adipose tissue accumulation that promotes insulin resistance and the development of type 2 diabetes mellitus (T2DM) (Liu et al., 2023). In addition to adipose tissue expansion, HFD also disrupts gut microbiota composition, leading to altered production of microbial metabolites. Gut microbiota-derived metabolites, such as short-chain fatty acids (SCFAs) and secondary bile acids, play a crucial role in mediating host microbiota crosstalk and regulating glucose and lipid metabolism as well as inflammatory responses. Dysregulation of these metabolites contributes to metabolic imbalance and exacerbates systemic inflammation, whereas their restoration has been shown to ameliorate HFD-induced obesity, hyperlipidemia, and hyperglycemia (Feng et al., 2023).

Furthermore, obesity is associated with increased infiltration and polarization of macrophages toward the pro-inflammatory M1 phenotype. These macrophages release cytokines such as TNF-α, IL-6, and IL-1β, which activate key inflammatory signaling pathways, including NF-κB and JAK/STAT, thereby amplifying chronic inflammation and promoting insulin resistance (Czaja-Stolc et al., 2022; Taylor, 2021).

Consistently, experimental studies have demonstrated that prolonged HFD exposure induces pancreatic islet remodeling and dysfunction, characterized by structural damage, reduced β-cell mass and secretory capacity, and downregulation of key islet-specific genes such as Ins1, Pdx1, and MafA. These alterations are accompanied by endoplasmic reticulum stress, extracellular matrix disruption, and shifts in gene expression profiles that collectively impair islet architecture and function, ultimately increasing susceptibility to T2DM (Wan et al., 2023).

2. Sedentary lifestyle

A sedentary lifestyle, characterized by prolonged sitting and low levels of physical activity, is a major contributor to insulin resistance and metabolic disorders. Insufficient physical activity reduces the expression and translocation of glucose transporter type 4 (GLUT4), impairing glucose uptake and metabolic homeostasis, while regular exercise has been shown to enhance GLUT4 activity for up to 72 hours and improve glucose regulation (Way et al., 2016).

Physical inactivity further exacerbates metabolic dysfunction by increasing pro-inflammatory cytokines such as IL-6 and TNF-α, reflecting a persistent low-grade inflammatory state that interferes with insulin signaling and lipid metabolism. Reduced myokine production, including irisin and brain-derived neurotrophic factor (BDNF), disrupts muscle–adipose tissue crosstalk and worsens obesity (Leal et al., 2018). In addition, mitochondrial dysfunction characterized by increased reactive oxygen species (ROS) and oxidative stress contributes to endothelial dysfunction and elevates the risk of metabolic syndrome (Kruk et al., 2019; Dikalov et al., 2023). Decreased activity of peroxisome proliferator-activated receptor gamma coactivator-1 alpha (PGC-1α), a key regulator of mitochondrial biogenesis, is also associated with insulin resistance (Rynders et al., 2018). Collectively, these alterations promote a pro-inflammatory state and metabolic imbalance, while regular physical exercise can mitigate these effects by reducing inflammation and improving mitochondrial function (Pinto et al., 2023).

3. Cigaratte smoking

Cigarette smoking is a prevalent lifestyle risk factor strongly associated with metabolic disorders. It disrupts metabolic homeostasis by reducing insulin sensitivity, enhancing inflammatory responses (Kim et al., 2020), and increasing oxidative stress (Tong et al., 2020), thereby promoting metabolic disease progression. At the gut level, chronic cigarette smoke exposure alters microbiota composition, characterized by increased abundance of Paraprevotellaclara, Clostridiales, and Ruminococcaceae, along with reduced levels of beneficial microbes such as Odoribacter and Roseburia hominis (Bai et al., 2022; Brown et al., 2023; Zhang et al., 2023). This dysbiosis increases intestinal permeability, facilitating endotoxin translocation and chronic low-grade inflammation, which subsequently impairs β-cell function and insulin secretion (Wu et al., 2025).

Nicotine exposure has been shown to induce pancreatic islet β-cell damage and impair regenerative capacity, ultimately leading to reduced insulin secretion (Sun et al., 2020). Mechanistically, nicotine exerts direct effects on pancreatic and peripheral metabolic tissues by suppressing glucose-stimulated insulin secretion, reducing insulin-like growth factor (IGF) levels, and inhibiting cyclin D1 expression, thereby promoting β-cell apoptosis. In addition, nicotine-induced oxidative stress disrupts mTOR–IRS1 signaling pathways in skeletal muscle and adipose tissue, resulting in decreased insulin sensitivity and elevated circulating free fatty acids. Despite these detrimental effects, activation of α7 nicotinic acetylcholine receptors (α7 nAChR) may confer partial protective effects through STAT3 signaling, attenuating TNF-α and triglyceride levels while supporting β-cell survival. Collectively, these findings highlight that smoking contributes to pancreatic dysfunction and insulin resistance through interconnected mechanisms involving oxidative stress, inflammation, gut microbiota

dysregulation, and impaired metabolic signaling (Artese et al., 2019; Xie et al., 2020; Gupta et al., 2018).

4. Alkohol Intake

The interaction between alcohol metabolism and glucose metabolism plays a critical role in the pathogenesis of type 2 diabetes mellitus (T2D). Alcohol metabolism increases the $NADH/NAD^+$ ratio, disrupting cellular redox balance and triggering oxidative stress and inflammatory responses that contribute to pancreatic β-cell damage, ultimately leading to insulin deficiency and resistance (Goodman et al., 2020; Cederbaum et al., 2009).

In the context of epigenetic regulation, alcohol-induced type 2 diabetes mellitus (T2DM) is closely linked to mitochondrial dysfunction in pancreatic β-cells. Chronic alcohol exposure promotes overactivation of the mitochondrial electron transport chain, particularly complex I, leading to excessive reactive oxygen species (ROS) production and redox imbalance. This oxidative stress damages mitochondrial structures, reduces ATP production, and induces endoplasmic reticulum (ER) stress, ultimately triggering β-cell apoptosis and functional decline (Tsang et al., 2022; Cortés-Rojo et al., 2020). These effects are further amplified by epigenetic alterations, including hypomethylation of the NDUFB9 gene, which destabilizes complex I and enhances ROS generation, as well as its interaction with ACTG1, linking mitochondrial dysfunction to cytoskeletal remodeling. Under hyperglycemic conditions, this redox imbalance is exacerbated, accelerating mitochondrial dysfunction and β-cell failure (Gao et al., 2019; Kim et al., 2024; Yau et al., 2021).

Alcohol also disrupts cellular signaling and metabolic regulation through hypermethylation of the SLC8A1 (NCX1) gene, impairing mitochondrial function and ATP synthesis (Syed et al., 2025; Li et al., 2025; Zhang et al., 2019). Additional regulators such as IGFBP7 and CCRL2 contribute to inflammation and insulin resistance (Xu et al., 2022). At the tissue level, non-oxidative metabolism of alcohol produces fatty acid ethyl esters (FAEEs), which initiate pancreatic injury, while ROS and acetaldehyde activate pancreatic stellate cells (PSCs), promoting fibrosis and structural remodeling (Petersen et al., 2021; Petersen et al., 2009).

Collectively, these mechanisms drive a pathological cycle of oxidative stress, inflammation, β-cell loss, and pancreatic fibrosis, accelerating T2DM progression. Notably, reduced β-cell regenerative capacity in East Asian populations may increase susceptibility to alcohol-induced β-cell dysfunction.

Pathophysiological Mechanisms of Air Pollution-Induced Pancreatic Dysfunction

1. Epidemiological Impact and Systemic Overview

Ambient air pollution is a major environmental risk factor associated with metabolic disorders, including type 2 diabetes mellitus (T2DM) (Honda et al., 2023; Nazarpour et al., 2023). Exposure to a complex mixture of pollutants specifically PM2.5, PM10, NO2, SO2, CO, and O3, primarily derived from industrial emissions and vehicle exhaust, has been linked to impaired glucose metabolism and progressive pancreatic dysfunction (Luo et al., 2024). Notably, fine particulate matter, SO2, and NOx show strong associations with increased GDM risk, although findings may vary due to differences in study design, exposure levels, and population characteristics (Zorena et al., 2022; Ren et al., 2023). Long-term particulate exposure is particularly concerning, as it has been reported to reduce insulin secretion capacity

by up to 30%, highlighting a substantial impact on pancreatic endocrine function (Liu et al., 2022).

2. Intracellular Stress and β-Cell Homeostasis

The underlying mechanisms of air pollution-induced damage are primarily driven by oxidative stress and chronic inflammation. Airborne particulate matter induces the production of pro-inflammatory cytokines, including TNF-α, IL-6, and VEGF. This is further exacerbated by adsorbed heavy metals including arsenic (As), cadmium (Cd), and lead (Pb), which amplify oxidative damage, induce lipid peroxidation, and disrupt trace element balance (Fouladi et al., 2020; Zorena et al., 2022).

At the cellular level, these processes disrupt mitochondrial and endoplasmic reticulum (ER) homeostasis, causing mitochondrial DNA damage and reduced ATP production. This cellular stress activates the unfolded protein response (UPR) pathways, specifically the PERK-eIF2α and IRE1-XBP1 axes. The sustained activation of these pathways impairs insulin biosynthesis, protein folding, and secretion, ultimately driving pancreatic β-cell apoptosis and reducing functional cell mass (Zorena et al., 2022; Ren et al., 2023).

3. Inflammasome Activation and RAS Dysregulation

Chronic exposure to fine particulate matter ($PM_{2.5}$) triggers local pancreatic injury through activation of the NLRP3 inflammasome and disruption of the renin–angiotensin system (RAS). Experimental models have shown that $PM_{2.5}$ exposure for approximately 12 weeks activates the NLRP3 inflammasome in pancreatic macrophages, leading to increased IL-1β expression and secretion, thereby sustaining a local inflammatorymicroenvironment.

Simultaneously, $PM_{2.5}$ shifts the RAS balance toward the deleterious Ang II/ACE/AT1R axis while suppressing the protective Ang-(1–7)/ACE2/MasR/AT2R pathway, which exacerbates oxidative stress, vascular dysfunction, and structural damage within pancreatic tissue. These local alterations are further reinforced by systemic inflammation, characterized by elevated IL-1β, TNF-α, and IL-17 levels, as well as gut microbiota dysbiosis that increases intestinal permeability and further disrupts metabolic homeostasis (Ferrario et al., 2022; Steckelings et al., 2022).

4. Extrapancreatic Influence: Adipose Tissue and Insulin Resistance

Beyond its direct effects on the pancreas, particulate matter (PM) exposure disrupts adipose tissue function, thereby exacerbating systemic insulin resistance. Circulating particles can infiltrate adipose tissue, activate resident macrophages, and trigger inflammatory responses characterized by increased production of pro-inflammatory cytokines such as TNF-α and IL-6. This inflammatory milieu alters adipokine secretion, leading to elevated leptin levels and reduced adiponectin expression. These hormonal changes suppress AMP-activated protein kinase (AMPK) activity, impair glucose uptake and fatty acid oxidation, and promote central leptin resistance, ultimately creating a vicious cycle of metabolic dysregulation (Della Guardia & Shin, 2022).

5. Integration of Lifestyle Factors and Air Pollution

Lifestyle-related factors and ambient air pollution exert synergistic effects on pancreatic dysfunction through overlapping biological pathways, including oxidative stress, chronic low-grade inflammation, gut microbiota dysregulation, and impaired metabolic signaling. Individually, unhealthy lifestyle behaviors such as cigarette smoking, excessive alcohol consumption, high-fat diet intake, obesity, and sedentary lifestyle have been consistently

shown to increase reactive oxygen species (ROS) production, elevate pro-inflammatory cytokines (e.g., TNF-α and IL-6), and impair insulin sensitivity, thereby promoting metabolic dysfunction (Bai et al., 2022; Brown et al., 2023; Wu et al., 2025).

At the molecular level, these factors disrupt insulin signaling pathways through abnormal phosphorylation of insulin receptor substrate-1 (IRS-1), inhibition of the PI3K/Akt pathway, and reduced translocation of glucose transporter type 4 (GLUT4) in peripheral tissues, ultimately leading to insulin resistance and impaired glucose homeostasis (Liu et al., 2022; Sun et al., 2022). In parallel, lifestyle-induced gut microbiota dysbiosis increases intestinal permeability, facilitating lipopolysaccharide (LPS) translocation and activation of systemic inflammatory responses, which further exacerbates β-cell dysfunction.

Concurrently, exposure to ambient air pollutants such as PM2.5, PM10, and NO_2 amplifies these pathological processes by inducing oxidative stress and activating innate immune pathways. Experimental studies have demonstrated that PM2.5 exposure upregulates NLRP3 inflammasome components and increases IL-1β expression, suggesting its role as a priming signal for inflammasome activation (Pinto et al., 2023; Kim et al., 2020). This priming is followed by secondary activation signals, including mitochondrial dysfunction, excessive ROS generation, potassium (K^+) efflux, and lysosomal destabilization, which promote inflammasome assembly and caspase-1 activation, leading to the maturation of IL-1β and IL-18.

Sustained activation of the NLRP3 inflammasome has direct consequences on pancreatic β-cells, including reduced insulin gene expression, impaired insulin secretion, and increased apoptosis (Liu et al., 2022). Additionally, both air pollution and unhealthy lifestyle factors disrupt mitochondrial and endoplasmic reticulum (ER) homeostasis, resulting in decreased ATP production and activation of unfolded protein response (UPR) pathways, particularly PERK–eIF2α and IRE1–XBP1 signaling, which further accelerate β-cell failure (Ren et al., 2023; Liu et al., 2022).

Beyond pancreatic effects, these exposures also target adipose tissue, where macrophage infiltration and pro-inflammatory cytokine production alter adipokine profiles. Increased leptin and reduced adiponectin levels suppress AMPK activity, impair glucose uptake, and promote systemic insulin resistance (Della Guardia & Shin, 2022). Importantly, the interaction between lifestyle factors and air pollution is synergistic rather than merely additive. For example, smoking-induced oxidative stress may be intensified by concurrent air pollution exposure, while pollution-related environmental constraints may reduce physical activity levels, reinforcing sedentary behavior (Xiang et al., 2022).

Furthermore, combined exposures exacerbate gut microbiota dysbiosis, increasing intestinal permeability and endotoxin translocation, which amplifies chronic inflammation and metabolic dysregulation. This integrated network of oxidative stress, inflammation, mitochondrial dysfunction, and immune activation creates a self-perpetuating pathological cycle that accelerates pancreatic β-cell damage and the progression of type 2 diabetes mellitus.

Collectively, these findings highlight that the convergence of environmental and behavioral risk factors significantly magnifies metabolic deterioration. Therefore, integrated preventive strategies targeting both lifestyle modification such as smoking cessation, reduced alcohol intake, improved diet, and increased physical activity and environmental interventions

to reduce air pollution exposure are essential to preserve pancreatic function and reduce the burden of T2D.

CONCLUSION

Pancreatic dysfunction and β-cell failure result from the combined effects of unhealthy lifestyle factors, including obesity, poor dietary patterns, smoking, and alcohol consumption, as well as environmental stressors such as $PM_{2.5}$ exposure. These factors activate overlapping pathological mechanisms, including oxidative stress, NLRP3 inflammasome activation, and endoplasmic reticulum stress. Collectively, these processes accelerate β-cell apoptosis and disrupt metabolic homeostasis, highlighting the need for integrated public health strategies that address both lifestyle modification and improvements in air quality.

Several limitations should be considered. Variations in pollution exposure levels and study designs across different regions make it challenging to establish a universal exposure threshold. Many findings are still derived from animal studies; therefore, further human-based research is required. In addition, evidence regarding the direct interaction between lifestyle factors and air pollution exposure in humans remains limited. Individual genetic variations and their potential influence on susceptibility to pancreatic dysfunction also require further investigation.

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