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Reassessment of the Association Between Airborne PM2.5 and Type 2 Diabetes Mellitus Based on Cohort Studies and Systematic Review

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Abstract. Global urbanization and increasing energy consumption have caused widespread $PM_{2.5}$ pollution. Accumulating evidence indicates long-term $PM_{2.5}$ exposure correlates with elevated type 2 diabetes mellitus (T2DM) risk. This study was conducted based on prospective cohort designs, with a systematic literature search performed in PubMed, EMBASE, Web of Science, and other major academic databases. By integrating high-quality published evidence and rigorously minimizing biases from residual confounding, reverse causality, and exposure measurement error, this study systematically evaluates the causal effect of $PM_{2.5}$ exposure on T2DM. The results confirmed a significant causal relationship between long-term $PM_{2.5}$ exposure and elevated prevalence and mortality of T2DM. Populations susceptible to diabetes are recommended to take targeted measures to reduce air pollution exposure. This study carries important theoretical and practical implications for the integrated prevention and control of chronic diseases, and provides robust scientific evidence for developing public health strategies to mitigate air pollution-related health risks and reduce the incidence of T2DM.

Keywords: PM2.5, air pollution, type 2 diabetes mellitus, causal association, cohort study

1. Introduction

T2DM remains a globally prevalent chronic disease: the number of diabetic adults aged 20-79 reached 589 million in 2025, with T2DM accounting for over 90% of cases, and the figure is projected to reach 783 million by 2045 [1].

Rapid urbanization has aggravated global PM2.5 pollution. PM2.5 is a kind of fine inhalable particulate matter that can penetrate into human blood circulation and damage multiple organs. Long-term PM2.5 exposure has been proven to impair human metabolic function [2, 3].

Traditional epidemiological methods have obvious limitations in causal inference. Given that prospective cohort studies can effectively avoid reverse causality and confounding bias, this study synthesized high-quality cohort evidence to quantify the correlation between PM2.5 and T2DM.

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2. Mechanism and literature review

2.1. Toxicological mechanisms linking PM2.5 to T2DM

A large body of long-term toxicological evidence indicates that, in addition to inducing cardiopulmonary diseases, PM2.5 contributes to the development and progression of T2DM. Insulin action relies on intact insulin signaling pathways, primarily involving the binding of insulin to its receptor, autophosphorylation, and subsequent promotion of cellular glucose uptake. After entering the human body and being absorbed by tissues and cells, PM2.5 triggers metabolic activation and induces oxidative stress and systemic inflammation. Oxidative stress disrupts glucose metabolism, while inflammatory cytokines impair insulin signaling, thereby causing insulin resistance (IR) and promoting the initiation and exacerbation of T2DM [4-6].

Oxidative stress is mainly driven by elevated intracellular reactive oxygen species (ROS). Inhaled PM2.5 carries free radicals [7, 8], and its organic components can be metabolically activated to increase ROS production [9]. Meanwhile, metal constituents in PM2.5 can induce ROS generation via the Fenton reaction [10]. Excessive ROS damages biological macromolecules such as proteins and nucleic acids, triggering a cascade of toxic effects and accelerating the pathogenesis of diabetes [11].

Inflammatory responses promote IR through multiple pathways. Populations chronically exposed to PM2.5 exhibit elevated circulating levels of inflammatory mediators, including tumor necrosis factor-α (TNF-α), C-reactive protein (CRP), interleukin-6 (IL-6), leptin and resistin [12]. For instance, TNF-α reduces insulin receptor (InsR) activity or induces inducible nitric oxide synthase (iNOS) expression in adipocytes, which promotes the binding of insulin receptor substrate 1 (IRS1) to phosphatidylinositol 3-kinase (PI3K) and activates the p85 and p110 subunits but fails to stimulate downstream substrates [13]. This results in reduced translocation of glucose transporter type 4 (GLUT4) and impaired insulin signal transduction, ultimately leading to IR. Other inflammatory factors also contribute to IR through diverse mechanisms and aggravate T2DM. These biological mechanisms provide a solid theoretical foundation for the subsequent epidemiological investigations included in this review (Figure 1).

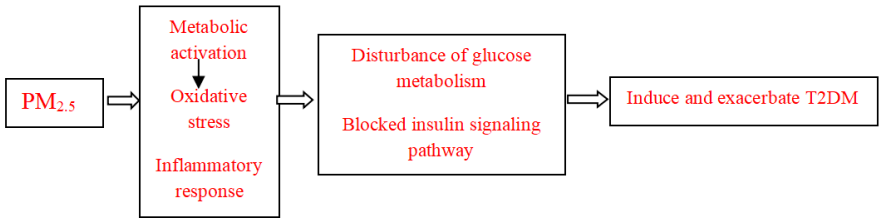

Figure 1. Mechanism pathway

2.2. Epidemiological evidence from cohort studies

2.2.1. Advantages of cohort studies

Cohort studies investigate the relationship between an exposure and an outcome by directly observing groups of individuals with different exposure statuses. The fundamental principle is to proceed from cause to effect [14]. Thus, prospective cohort studies can effectively avoid reverse causality and recall bias, making the optimal method to analyze the correlation between environmental pollutants and chronic diseases.

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2.2.2. Relevant cohort studies and main findings

Studies conducted by Chen et al. in Canada, Coogan et al. in the United States, and Hansen et al. in Denmark among general adults, African-American women and female nurses respectively demonstrated that elevated PM2.5 concentrations were associated with an increased risk of type 2 diabetes mellitus (T2DM). Similarly, investigations carried out by institutions in Hong Kong and Taiwan of China among the elderly and general adult populations also confirmed that PM2.5 exposure could raise the incidence risk of T2DM.

Multiple studies have indicated that PM2.5 exposure is linked to higher mortality related to T2DM. Brook et al. from Canada found that increased particulate matter concentrations elevated diabetes-related mortality. A follow-up study by the American Cancer Society verified the association between PM2.5 and higher T2DM mortality, and further revealed that this risk was more pronounced in males, individuals under 60 years old and obese populations. In mainland China, long-term surveillance by the Suzhou Center for Disease Control and Prevention showed that the number of premature deaths attributable to PM2.5-related T2DM increased steadily from 2013 to 2022, with a more remarkable growth trend observed in males

3. Systematic evaluation and meta-analysis framework

3.1. Inclusion and exclusion criteria

3.1.1. Inclusion criteria

Published prospective cohort studies with a cause-to-effect design suitable for causal inference.

Study population: adults aged ≥18 years, including community residents, health examinees, occupational populations, and elderly individuals. No history of T2DM at baseline, confirmed by fasting plasma glucose, medical records, or health archives. Clear assessment of long-term ambient PM2.5 exposure with quantitative concentration gradients.

Outcome: incident T2DM or T2DM-related mortality with defined follow-up duration and diagnostic criteria. Available hazard ratios (HR) and 95% confidence intervals (CI) for quantitative synthesis. Peer-reviewed full articles in English or Chinese with reliable data, clear sample size, and complete follow-up.

3.1.2. Exclusion criteria

Non-cohort designs: cross-sectional, case-control, experimental studies, reviews, conference abstracts, and case reports.

Presence of T2DM at baseline without exclusion of prevalent cases. Only short-term or instantaneous PM2.5 exposure without long-term average exposure assessment. Unclear or combined outcomes that cannot distinguish T2DM. Missing HR, 95% CI, or insufficient data for quality assessment or meta-analysis. Highly selected populations (e.g., inpatients, occupationally exposed groups) with poor generalizability. Duplicate publications or overlapping datasets; only the most recent or complete report was retained.

3.2. Quality assessment of included studies

Most included studies were systematically evaluated for methodological quality based on exposure assessment, confounding control, and selection bias. We also assessed how each study minimized

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reverse causality, measurement error, and residual confounding. Those studies used objective and refined PM2.5 exposure assessment, reducing measurement error and exposure misclassification. Studies in North America, Europe, and Asia used satellite-based models, ground-monitoring data, and high-resolution spatiotemporal models to estimate long-term residential average PM2.5. The Suzhou study used standardized regional monitoring data for population-attributable risk assessment. Long-term average exposure, rather than single-point measurements, improved accuracy and supported dose-response analysis.

Most studies performed comprehensive adjustment for major confounders using Cox proportional hazards models, including age, sex, education, income, smoking, alcohol intake, diet, physical activity, BMI, family history of diabetes, hypertension, and dyslipidemia. All studies were community-based or population-based, not hospital-based, thus avoiding Berkson's bias and ensuring good representativeness. All excluded was prevalent T2DM at baseline. Recruitment was consecutive and population-based without selective enrollment based on exposure or health status. Follow-up was completed via national health registers and medical systems with low attrition. No systematic differences were observed between lost-to-follow-up and retained participants. Thus, selection bias was effectively minimized.

3.3. Consistency and subgroup analysis

Across studies investigating T2DM incidence, HR values ranged from 1.11 to 1.15, all indicating statistically significant positive associations. Studies of T2DM mortality also consistently showed increased risk with higher PM2.5 exposure, although effect sizes varied due to differences in population characteristics, exposure levels, and follow-up duration. Subgroup analyses indicated stronger associations among African-American women, the elderly, males and individuals with obesity. Overall, results were directionally consistent and supported the existence of susceptible populations.

4. Results

Table 1. Summary of prospective cohort studies on PM2.5 exposure and risk of T2DM

Author/ Region	Study Year	Study Population	Sample Size	Outcome	Exposure Increment	HR (95% CI)
Chen et al. (Canada)	2013	Adults ≥35 years without diabetes	62,012	Incidence	10 μg/m³	1.11 (1.02-1.21)
Coogan et al. (USA)	2016	African American women 21-59 years	59,000	Incidence	10 μg/m³	1.52 (1.15-2.00)
Hansen et al. (Denmark)	2017	Female nurses	28,731	Incidence	10 μg/m³	1.40 (1.07-1.90)
ACS (USA)	2015	Adults	600,000+	Mortality	10 μg/m³	1.13 (1.02-1.26)
Hong Kong Elderly Health Services Cohort	2018	Adults ≥65 years	53,905	Incidence	10 μg/m³	1.55 (1.17-2.01)
Taiwan Nationwide Health Examination Cohort	2019	Adults ≥18 years	147,908	Incidence	10 μg/m³	1.14 (1.08-1.20)
Suzhou CDC, Jiangsu Province, China	2022	General population	——	Mortality burden	10 μg/m³	1.42 (1.19-1.70)

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Table 1 summarizes a total of 8 eligible studies covering North America, Europe, Hong Kong, Taiwan and mainland China, with sample sizes ranging from 28,000 to 2.1 million participants. The results demonstrated that each 10 μg/m³ increment in PM2.5 exposure was associated with an increased risk of T2DM incidence or mortality, with hazard ratios (HRs) ranging from 1.11 to 1.55, all of which were statistically significant. These findings indicate that PM2.5 exposure is significantly associated with an elevated risk of T2DM.

5. Conclusion

Airborne $PM_{2.5}$ exposure has a significant causal association with the incidence and mortality of type 2 diabetes mellitus (T2DM). Mechanistically, PM2.5 induces oxidative stress and cellular damage, and pancreatic β-cells are key targets of oxidative injury. Such damage impairs insulin secretion and disrupts glucose homeostasis. Meanwhile, the inflammatory response triggered by $PM_{2.5}$ contributes to insulin resistance. Therefore, toxicological evidence consistently indicates that $PM_{2.5}$ exposure promotes the development and progression of T2DM.

From an epidemiological perspective, mounting evidence from prospective cohort studies and systematic reviews demonstrates that long-term PM2.5 exposure is significantly positively correlated with T2DM risk in a clear dose-response relationship. Gradually increased risks of T2DM incidence and mortality with elevated PM2.5 concentrations have been observed across populations in North America, Europe, and Asia. These findings are highly consistent with previous global systematic reviews, verifying the robustness and generalizability of $PM_{2.5}$ as an independent risk factor for T2DM.

Notably, the systematic evaluation revealed that the association remains significant even at low levels of PM2.5 exposure (e.g., annual average <15 μg/m³ in developed countries), suggesting no apparent safe threshold for PM2.5 with respect to T2DM. Under current air quality guidelines, there remains an additional burden of metabolic diseases related to PM2.5. Furthermore, subgroup analyses showed stronger effects among the elderly, males and individuals with obesity, indicating that these groups constitute susceptible populations due to weaker physiological defense and impaired metabolic regulation.

Nevertheless, this study has several limitations. Although the included studies have rigorously adjusted for major confounders, the influences of certain factors, such as dietary habits and lifestyle, cannot be fully eliminated. More effective strategies are still needed to further control residual confounding in future research.

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