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AIR POLLUTION AND DIABETES: A NARRATIVE REVIEW OF AVAILABLE META-ANALYSIS

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Evidences gathered until now regarding the relationship between air pollution and health outcomes mainly refer to respiratory diseases, cardiovascular, adverse birth outcomes, and cognitive function. Diabetes, a common chronic condition with an alarming increase worldwide, is also sought to be related to air pollution among other various factors. Our review of data linking air pollution and diabetes based on published meta-analysis between 2018 and 2023 confirm that exposure to air pollutants is associated with increased risk of prevalent and incident type 2 diabetes and with increased risk of gestational diabetes. Air pollution represents a novel risk factor that should be targeted when comprehensive prevention strategies are designed to attenuate the epidemics of diabetes worldwide.

Keywords: air pollution, diabetes, gestational diabetes, meta-analysis.

INTRODUCTION

Noncommunicable diseases (NCDs) are now responsible for 74% of death globally and are represented by cardio- and cerebrovascular diseases, cancer, diabetes, and chronic respiratory diseases. The common soil of NCDs is represented by several key modifiable risk factors like tobacco use, unhealthy diet, low physical activity level, and the harmful use of alcohol, all leading to a constellation of other risk factors/ diseases such as overweight and obesity, high blood pressure, and high cholesterol[1]. These conventional risk factors act in a milieu of other conditions – genetic factors such as genetic inheritance, epigenetic changes, or mutations induced by radiation and exposure to toxic substances; socio-demographic factors such as age, gender, race, ethnicity, education and income and environmental factors such as climate changes, UV radiation and ambient and household air pollution[2].

A growing body of evidence is showing that acute and chronic exposure to air pollution increases the morbidity and mortality in humans[3]. According to the World Health Organization (WHO), over 4 million deaths can be attributed every year to ambient (outdoor) air pollution and 91% of the world population lives in areas where air quality guidelines levels were not met[4] urging WHO to issue new guidelines for air quality in 2021[5].

Different contaminants are responsible for air pollution, amongst which the following are the most common: particulate matter (PM), ground-level ozone (O_3), carbon monoxide (CO), sulfur dioxide (SO_2), and nitrogen dioxide (NO_2). PM are characterized as the mass, in a given air volume, of all the particles with an aerodynamic diameter below a certain level. The most widely known are $PM_{2.5}$ and PM_{10}, with an aerodynamic diameter below 2.5 μm and 10 μm, respectively[3,5].

Evidence gathered until now regarding the relationship between air pollution and health outcomes mainly refer to respiratory diseases-asthma and chronic obstructive pulmonary disease (COPD), cardiovascular - mostly stroke, adverse birth outcomes, and cognitive function[3]. Diabetes, a common chronic condition with an alarming increase worldwide[6], is also sought to be related to air pollution among other various factors[7]. Therefore, we aimed to perform a review of data linking air pollution and diabetes based on meta-analyses published between 2018 and 2023.

MATERIALS AND METHODS

For the purpose of this report, we conducted a systematic search of meta-analyses published during the last five years. Meta-analyses were chosen due to the high level of evidence as represented by the evidence-based pyramid[8]. Although passive smoking is an aspect of air pollution, it was excluded from the analysis due to the large body of evidence already available.

DATA SOURCES, SEARCH STRATEGIES AND STUDY SELECTION

EMBASE and PUBMED databases were searched with the terms ’air pollution’ AND ’diabetes mellitus’ and the search criteria were restricted to meta-analysis and to years 2018 to 2023. Duplicates were removed and the remaining publications were screened by two independent reviewers for relevance based on the title and abstract first, and then based on full text. Disagreements between reviewers were mediated until a final decision to retain or to exclude the study was reached. The main aspects of each selected meta-analyses were described by type of diabetes (all types, type 2, type 1 and gestational diabetes).

RESULTS AND DISCUSSIONS

The database search identified a total of 63 records (29 in EMBASE and 34 in PUBMED). After removing the duplicates, 59 records were examined for the relevance to the study objectives. Thirty records were excluded after screening of the title and abstract for not addressing study question (did not report diabetes as outcome or were not meta-analyses), and the remaining 29 were retrieved in full-text for further assessment. The final analysis included 11 meta-analyses relevant for the objective of this review (Figure 1).

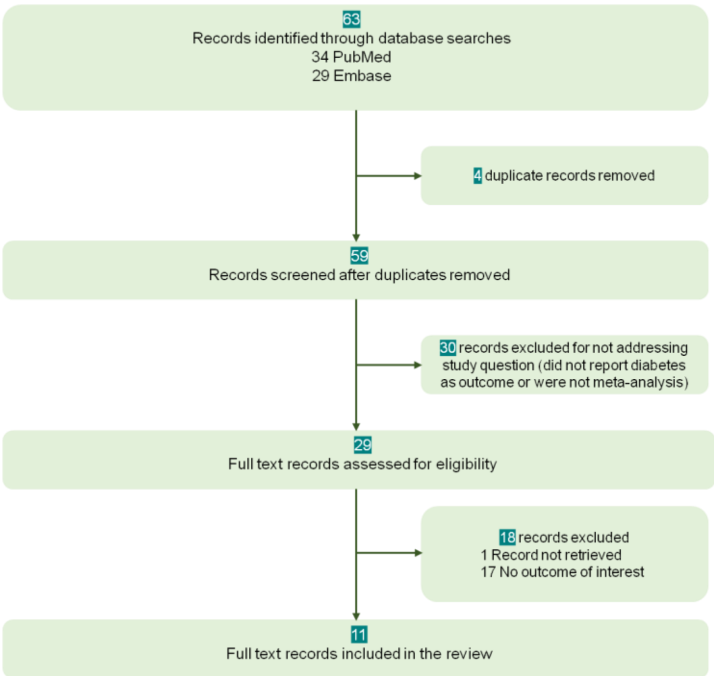

Figure 1. Study selection flowchart.

DIABETES (ALL TYPES)

Only 2 meta-analyses evaluating the impact of air pollution on risk of all types of diabetes were found.

The meta-analysis of Kutlar Joss M. et al., 2023 examined the association between traffic-related air pollution (TRAP) and risk of diabetes (all types)[9]. TRAP is a complex mixture of pollutants from tailpipe containing PM and nitrogen oxides and non-tailpipe originating from brake, tire, and road surface abrasion, and re-suspension of dust and include PM trace metals such as copper (Cu), iron (Fe) and zinc (Zn). The meta-analysis selected 21 studies and found that all TRAP were significantly associated with the prevalence and incidence of diabetes, with NO_2 being the most studied (relative risk [RR] = 1.09; 95% confidence interval [CI]: 1.02; 1.17 *per* 10 μg/m^3 for prevalence and RR = 1.04; 95% CI: 0.96; 1.13 per 10 μg/m^3 for incidence of diabetes). No sub-analysis was performed for type of diabetes.

The meta-analysis of Mohanannair Geethadevi G. *et al*., 2023[10] examined the effect of O_3 on the risk of type 1, type 2, and gestational diabetes and selected 19 studies- three on type 1 diabetes, five were on type 2 diabetes, and eleven were on GDM. O_3 exposure was positively correlated with type 2 diabetes [effect size (ES) = 1.06, 95% CI: 1.02, 1.11] and gestational diabetes [pooled odds ratio (OR) = 1.01, 95% CI: 1.00, 1.03], with the risk of gestational diabetes occurring if the exposure occurred in the first trimester. No significant association was observed between O_3 exposure and type 1 diabetes.

TYPE 1 DIABETES

No meta-analysis specifically addressed to type 1 diabetes was found, except that published by Mohanannair Geethadevi G. *et al*.

TYPE 2 DIABETES

The meta-analysis of Liu F. *et al*., 2019 included 30 studies from mostly from United States and Europe[11]. The pooled results showed that higher levels of air pollution exposure were modestly but significantly associated with higher prevalence of type 2 diabetes for all types of pollutants: per 10 μg/m^3 increase in concentrations of $PM_{2.5}$: OR = 1.09, 95%CI: 1.05, 1.13; PM_{10}: OR = 1.12, 95%CI: 1.06, 1.19; NO_2: OR = 1.05, 95%CI:1.03, 1.08). Higher type 2 diabetes incidence was found only for $PM_{2.5}$ exposures (per 10 μg/m^3 increase in concentration of $PM_{2.5}$: hazard ratio (HR) = 1.10, 95%CI:1.04, 1.16, and not with PM_{10} and NO_2. No significant difference between high-income countries and low- and middle-incomes countries and prevalent type 2 diabetes were observed. No significant differences were found between females and males, except for the effect of NO_2 on type 2 diabetes incidence which was stronger among females.

Similar results were reported by the meta-analysis of Yang B.Y. *et al*., 2020 which included 86 studies[12]. The results showed that $PM_{2.5}$, PM_{10} and NO_2 exposure was significantly associated with prevalent type 2 diabetes, while $PM_{2.5}$, PM_{10} but not NO_2 were also associated with incident type 2 diabetes. The magnitude of the effects was also similar, with a ≈10% increased risk per 10 μg/m^3 increase in concentrations.

Yang M. *et al*., 2020 performed a meta-analysis examining specifically the relationship between ambient pollution and incidence of type 2 diabetes[13], with a stratified analysis by regions of the studies and length of follow-up. Sixteen studies with 18 cohorts were included. The incidence of type 2 diabetes was significantly associated with 10 μg/m^3 increase of $PM_{2.5}$ (overall HR = 1.11, 95% CI: 1.03, 1.19) and PM_{10} (overall HR = 1.12, 95% CI: 1.01, 1.23) exposure. In further analysis $PM_{2.5}$ was significantly associated with increased type 2 diabetes incidence in American countries but not European countries. In the long follow-up cohorts, it was also confirmed that exposure to $PM_{2.5}$ and PM_{10} was associated with increased diabetes incidence. Additionally, educational level and gender could potentially affect the impacts of PM_{10} and $PM_{2.5}$ on diabetes incidence.

A systematic review and meta-analysis published by Chen Z. *et al*. in 2022[14] evaluated the quantitative concentration-response relationships between indoor exposure to SO_2, NO_2, O_3, and carbon monoxide (CO) and various health outcomes including diabetes. A total of 19 health outcomes in 101 studies with 182 health risk estimates were examined in this report. Only NO_2 (per 10 μg/m^3) was associated with diabetes with a pooled RR of 1.019 (95% CI 1.009–1.029).

GESTATIONAL DIABETES

The systematic review and meta-analysis of Bai W. *et al*., 2020[15] examined the association between ambient air pollutants ($PM_{2.5}$, PM_{10}, CO, NO, NO_2, NO_x, O_3, and SO_2) and pregnancy complications (gestational diabetes, hypertensive disorders of pregnancy, preeclampsia, and gestational hypertension). It included 33 cohort studies conducted on 22,253,277 pregnant women. Meta-analyses showed that during the first trimester, there were significant associations of SO_2 with gestational diabetes (RR = 1.04, 95% CI: 1.00–1.08 *per* 1 ppb increment, I^2 = 54.1%), but not of PM or other contaminants.

The meta-analysis published by Hu G.Y. *et al*., 2020 included a total of 11 studies evaluating the association between gestational diabetes and exposure to air pollution[16]. The summary OR for incidence of gestational diabetes following a 10 μg/m^3 increase in $PM_{2.5}$ exposure during the second trimester was 1.04 (95% CI: 1.01, 1.09) and in NO_x during the first trimester was 1.03 (95%CI: 1.00, 1.07) per 10 ppb increase, while for high versus low SO_2 exposure during the second trimester was 1.25 (95%CI: 1.02, 1.53). There was a high heterogeneity among results in majority of the analyses which were attributed to different exposure assessment methods, different populations and geographical areas, and covariates adjustment.

Zhou X. *et al*., 2022 performed a meta-analysis including 20 cohort studies with stratified analyses by study regions and units of pollutant increase and with sensitivity analyses to assess the robustness[17]. It confirms that there is a clear association between $PM_{2.5}$, PM_{10}, NO_2, and SO_2 exposure increased the risk of gestational diabetes. Interestingly, exposure to O_3 was associated with reduced risk of gestational diabetes with a pooled effect estimate of 0.635. According to exposure period, $PM_{2.5}$ exposures in the first and second trimesters, and NO_2 and SO_2 exposure in the first trimester significantly increased the risk of gestational diabetes, with the RR ranging from 1.015 to 1.032. The risk related to air pollution was more pronounced in Asian subjects than in American subjects.

In 2023, Nazarpour S. *et al*.[18] published an updated meta-analysis of 13 studies examining 2,826,544 pregnant women which showed that $PM_{2.5}$, PM_{10}, O_3, and SO_2 exposure increased the risk of gestational diabetes by 9, 17, 10 and 10% respectively compared with non-exposure.

Another meta-analysis from 2023 published by Liang W. *et al*.[19] confirmed that exposure to $PM_{2.5}$, PM_{10}, SO_2, and NO_2 was associated with increased risk of gestational diabetes, especially when exposure occurred in the pre-conception and first trimester of pregnancy. The components of $PM_{2.5}$ were further analyzed and was found that the risk was strongly linked to black carbon (BC) and nitrates (NO_3^-). Another finding was that there was a stronger correlation of gestational diabetes risk with higher levels of pollutants in Asia, except for $PM_{2.5}$ and BC, which suggested that the specific composition of particulate pollutants had a greater effect on the exposure-outcome association than the concentration.

Our review of the literature based on published meta-analyses confirmed that air pollution was associated with the risk of diabetes – mainly type 2 and gestational diabetes, and that air pollution should be targeted as a novel risk factor susceptible, if ameliorated, to contribute to diabetes prevention. Several mechanisms were described in relation to the effect of different air pollutants on glucose metabolism and further on the development of chronic hyperglycemia/ diabetes.

Several PM species have been identified as endocrine disrupting chemicals which were linked to insulin resistance, elevated circulating adipokines, hypothyroidism and (mixed) estrogenic effects. PM are associated with increased oxidative stress, inflammatory response, and dyslipidemia, which in turn contribute to insulin resistance and non-alcoholic steatosi, known contributers to progression of chronic hyperglycemia[20, 21].

During pregnancy, it is thought that preconception exposure to ambient air pollution may aggravate beta cell dysfunction in the context of physiological insulin resistance and accelerate the progression of gestational diabetes. Moreover, exposure to $PM_{2.5}$ in the first trimester has been confirmed to increase the level of placental global DNA methylation which in turn is related with diabetes risk[22].

CONCLUSION

Exposure to air pollutants is associated with aggravated risk for type 2 diabetes and gestational diabetes, representing a novel risk factor that should be targeted when comprehensive prevention strategies are designed to attenuate the epidemics of diabetes worldwide.

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