The Association between Exposure to Air Pollution and Type 1 Diabetes Mellitus: A Systematic Review and Meta-Analysis

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Abstract

Background: This systematic review and meta-analysis aimed to overview the observational studies on the association of exposure to air pollution and type 1 diabetes mellitus (T1DM).

Materials and Methods: Based on PRISMA guidelines, we systematically reviewed the databases of PubMed, Scopus, Embase, and Web of Science databases to determine the association of air pollution exposure and T1DM. Quality assessment of the papers was evaluated using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist for observational studies. The odds ratios (OR) and their 95% confidence intervals (CI) were calculated to assess the strength of the associations between air pollutants (gases and particulate matter air pollutants including PM10, PM2.5, NO2, volatile organic compound, SO4, SO2, O3) and T1DM.

Results: Out of 385 initially identified papers, 6 studies were used for this meta-analysis. Fixed effects meta-analysis showed a significant association between per 10 μg/m^3 increase in O3 and PM2.5 exposures with the increased risk of T1DM (3 studies, OR = 1.51, 95% CI: 1.26, 1.80, I^2 = 83.5% for O3 and two studies, OR = 1.03, 95% CI: 1.01, 1.05, I^2 = 76.3% for PM2.5).There was no evidence of association between increased risk of T1DM and exposure to PM10 (OR = 1.02, 95% CI: 0.99–1.06, I^2 = 59.4%), SO4 (OR = 1.16, 95% CI: 0.91–1.49, I^2 = 93.8%), SO2 (OR = 0.94, 95% CI: 0.83–1.06, I^2 = 85.0%), and NO2 (OR = 0.995,95% CI: 1.05–1.04, I^2 = 24.7%).

Conclusion: Recent publications indicated that exposure to ozone and PM2.5 may be a risk factor for T1DM. However, due to limited available studies, more prospective cohort studies are needed to clarify the role of air pollutants in T1DM occurrence.

Keywords: Adolescents, air pollution, children, meta-analysis, type 1 diabetes mellitus

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Introduction

Type 1 diabetes mellitus (T1DM) is one of the most common chronic diseases in children. It accounts for approximately 10% of the total diabetic cases that stems from the autoimmune destruction of insulin-producing pancreatic beta cells and leads to lack or insufficient insulin secretion.[1,2]

Epidemiologic studies indicated a 2%–5% increasing trend for T1DM worldwide. The causes of this increasing rate have

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not been determined yet.[3] Numerous prospective studies have been conducted so far to understand the etiology of T1DM, but no definitive answers have been reached. Genetic factors have been demonstrated to play profound roles in T1DM development.[4] However, data from identical twins show that there might be other non-genetic factors (such as environmental triggers) that initiate the disease process and act together with genetic factors in T1DM development and progression.[5] In this regard, more recent studies have highlighted the potential impact of exposure to air pollution on the increased prevalence and mortality of T1DM.[6]

Air pollution has been recognized as the most important environmental health risk factor globally, leads to 4.6 million deaths annually according to the World Health Organization.[7] Based on their state in the atmosphere, air pollutants comprised both gaseous and particulate matters (PMs) which include compounds of ozone, sulfur, nitrogen, carbon oxides, hydrocarbons, halogens, and total suspended PMs, inhalable PM10, fine PM2.5, and ultrafine PM.[8] Several epidemiological studies have demonstrated a link between exposure to one or some of these air pollutants and adverse human health effects including respiratory diseases, cerebrovascular diseases, and cardiovascular diseases.[9] Similarly, in recent years, accumulating evidence suggest that exposure to these air pollutants (ambient and outdoor) increases the risks of several autoimmune disorders, including diabetes[9]. More recent studies also reported some mechanisms of air pollutants in developing immune disorders.[10,11]

Although previous studies have revealed an association between exposure to air pollution and T2DM,[12] no conclusive relationship has been found for air pollution exposure and the development or progression of T1DM. In this regard, some studies have shown that prenatal exposure to air pollution may be associated with a higher risk of offspring T1DM.[13] Moreover, higher risk of T1DM incidence has been reported in countries by higher concentrations of PM10 <10μm, nitrogen oxides, (NOx), and nonmethane volatile organic compounds (VOCs) emissions.[14] Several other investigations have also implicated that cumulative exposure to specific air pollutants may predispose to the development of T1DM in children.[15] Furthermore, in another study conducted in the USA, the authors concluded that exposure to ambient pollutants like ozone may contribute to T1DM development, while exposure to PM[12] might be associated with T1DM before 5 years of age.[16] In contrast to the mentioned researches, there are also other studies showing no association between exposure to air pollution with T1DM development or its metabolic control.[17]

Based on the mentioned notes, it is controversial whether there is any relationship between exposure to air pollution and the risk of T1DM. Therefore, in the present study, we attempted to systematically review the literature to identify any relationship between exposure to a wide array of gaseous and particulate air pollutants with T1DM. To the best of our knowledge, this is the first effort aimed to examine the overall association of air pollution and the risk of T1DM through a meta-analysis and literature review.

Materials and Methods

Search strategy

In this systematic review study, the literature was searched in PubMed, Scopus, Embase, and Web of Science databases until May 2020. All cross-sectional, case–control, and cohort studies were considered. The search strategy used in the databases was as follows: ("Air Pollutions" OR "Pollution, Air" OR "Air Quality" OR "air contamination" OR "air pollution" OR "air pollutioning" OR "atmosphere pollution" OR "atmospheric pollution" OR "polluted air" OR "polluted atmosphere") in combination with ("Type 1 Diabetes Mellitus" OR "Diabetes Mellitus, Type I" OR "Type 1 Diabetes" OR "Diabetes, Type 1" OR "Diabetes Mellitus, Ketosis-Prone" OR "Diabetes Mellitus, Ketosis Prone" OR "Ketosis-Prone Diabetes Mellitus" "Diabetes, Autoimmune" OR "Autoimmune Diabetes" OR "Diabetes Mellitus, Juvenile-Onset" OR "Diabetes Mellitus, Juvenile Onset" OR "Juvenile-Onset Diabetes Mellitus" OR "Juvenile-Onset Diabetes" OR "Diabetes, Juvenile-Onset" OR "Juvenile Onset Diabetes" OR "Diabetes Mellitus, Insulin-Dependent" OR "Diabetes Mellitus, Insulin Dependent" OR "Insulin-Dependent Diabetes Mellitus" OR "IDDM" OR "Diabetes Mellitus, Insulin-Dependent, 1" OR "Insulin-Dependent Diabetes Mellitus 1"OR "Insulin-Dependent Diabetes Mellitus 1" OR "Diabetes Mellitus, Brittle" OR "Brittle Diabetes Mellitus" OR "Diabetes Mellitus, Sudden-Onset" OR "Diabetes Mellitus, Sudden Onset" OR "Sudden-Onset Diabetes Mellitus" OR "ketoacidotic diabetes" OR "labile diabetes mellitus" OR "mckusick 22210"OR "T1DM") AND (child OR adolescent OR school-aged OR youth OR teenager OR boy OR girl OR student OR pediatrics). Relevant articles were obtained without any language restriction. In addition, references of the relevant papers were screened to further identify eligible papers manually. All the retrieved publications were entered into reference-manager software (EndNote X7, Thomson Scientific, Stamford, CT, USA).

Study selection

Studies included if they met the following criteria: (i) observational study (ii) participants: children and adolescents; (iii) main outcome was T1DM; (iv) reporting the odds ratio (OR), hazard ratio (HR), relative risk (RR) or β-coefficient of air pollutions with T1DM. In this study, we focused on gaseous pollutants PM_{10}, $PM_{2.5}$, O_3, SO_2, NO_2, and VOCs. Studies reporting duplicated results and studies with low quality were excluded.

Data extraction and quality assessment

Two reviewers screened the retrieved literatures by title and abstracts and then, full texts were assessed independently based on inclusion criteria. Information was extracted from

the studies included the first author's name, year, country, number of participants and cases of diabetes and study design, follow-up period (for cohort studies), participants' characteristics (age and gender), exposure measurement, covariates, and study results.

Two investigators (NM and MY) independently assessed the quality of eligible studies according to the checklist from STROBE in which the studies were divided into three groups of high, medium, and low quality.

Different results of the quality assessment were resolved by consultation and consensus.

Statistical analysis

As this meta-analysis aimed to investigate the relationship between air pollution and T1DM in children. The effect sizes of the RR, OR, and HR. RR and HR were considered as OR because incidence and prevalence of T1DM is low in the children.[18] The units of measurement of air pollution in the individual studies were μg/m^3 or ppb. To coordinate the air pollution unit, we converted ppb to μg/m^3. The OR of T1DM was calculated for a 10-μg/m3 increase in air pollutant concentration for $PM_{2.5}$, PM10, NO2, and O_3, and for a 1-μg/m^3 increase in SO_4 and SO_2.[15,16]

A pooled effect size was estimated if there were two or more studies that adopted the same exposure. Heterogeneity across the enrolled studies was evaluated by Cochran's Q-statistic and I^2 statistic was used to estimate the heterogeneity of the studies in the meta-analysis.[19] Standard random-effects meta-analysis methods perform poorly when applied to few numbers studies.[20] Therefore, for synthesizing specific ORs for each pollutant we used fixed-effect method. Funnel plot asymmetry tests were performed to assess the potential publication bias.[21] Two-tailed $P < 0.05$ was considered statistically significant. All analyses were performed using STATA version 14.0 ((StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP.).

Results

Search results and quality assessment

In the primary search based on the terms, 385 literatures were identified from electronic databases.

(PubMed, Embase, Web of Science, Cochrane Library and Scopus) and manual search. Subsequently, 12 studies were remained after the removal of duplicates and irrelevant titles and/or abstracts (13-18, 22-27). By reviewing the full text of articles, a total of six studies met the inclusion criteria in the current meta-analysis (15, 16,24-27), and others were removed for the following reasons: studies with insufficient data, reviews, non-human studies, and studies unrelated to this meta-analysis [Figure 1]. We excluded one case-control study because it evaluated prenatal exposures to air pollutants and the later development of T1DM in children.[13] We also excluded one study because it did not report the measure of association between air pollution and the risk of T1DM in children and adolescents.[22] A population-based study also was excluded because the air pollution was measured as Tonnes of emissions per year.[14] Additional two studies were excluded due to insufficient data to extract the effect size.[22,23]

Studies were conducted from European and American countries. The characteristics of the included studies are summarized in Table 1 (14-16, 24-27). Overall, the studies were published between 2002 and 2020. We selected six studies for extracting data and quality assessment.

The association between Type 1 Diabetes and PM_{10} and O_3 exposure was assessed in three studies. Two studies reported the effects of SO_4, SO_2, and $PM_{2.5}$ exposure, and four studies reported the effects of NO_2 exposure on T1DM incidence.

Figure 2 and Table 2 shows the pooled results of association (95% CI) for all 16 effect estimates from 6 studies. It showed that air pollution exposure was not associated with T1DM. Overall effect size was statistically significant (OR = 1.05, 95% confidence interval [CI]: 0.99, 1.11, $I^2 = 78.9\%$).

We investigated the association of each particular matter with T1DM risk in separate meta-analyses [Figure 3]. Because of the small number of studies for each pollutant, we used a fixed-effect meta-analysis (<5). The individual study results and the pooled effect sizes of OR (by pollutants) are shown in Figure 3.

With regard to exposure to PM_{10} pollutants of three effect sizes, the pooled results using the fixed-effect model did not show a significant association (OR = 1.02, 95% CI: 0.99, 1.0, $I^2 = 59.4\%$).

In an analysis restricted to the O_3, two effect sizes found a statistically significant association between O_3 and T1DM; the pooled estimated OR using the fixed-effect model was 1.62 (95% CI: 1.24, 2.12) and the test for heterogeneity was statistically significant ($I^2 = 91.5\%$; $P_{heterogeneity} \leq 0.001$).

In a fixed-effect model meta-analysis restricted to the $PM_{2.5}$, the pooled estimated OR was 1.03 (95% CI: 1.01, 1.05) and the test for heterogeneity was statistically significant ($I^2 = 76.3\%$; $P_{heterogeneity} \leq 0.04$). In contrast, random-effect model meta-analysis showed no significant association (OR = 0.71, 95% CI: 0.28, 1.79).

There was no evidence for the association between exposure to air pollution (NO_2, SO_2, and SO_4) and T1DM risk. The pooled effect using the fixed-effect model was 1.00 (95% CI: 0.95–1.04) for NO_2, 0.94 (95% CI: 0.83–1.06) for SO_2, 1.16 (95% CI: 0.91–1.49) for SO_4. The degree of heterogeneity (I^2) in the current meta-analysis for NO_2, SO_2, and SO_4, were 24.7%, 85%, and 93.8%, respectively [Figure 3].

Publication bias

Funnel plot showed no publication bias in our meta-analysis [Figure 4]. Begg's adjusted rank correlation ($z = -0.27$, $P = 0.79$) and Egger's regression asymmetry test ($t = 0.25$, $P = 0.81$) did not inferred to publication bias, too.

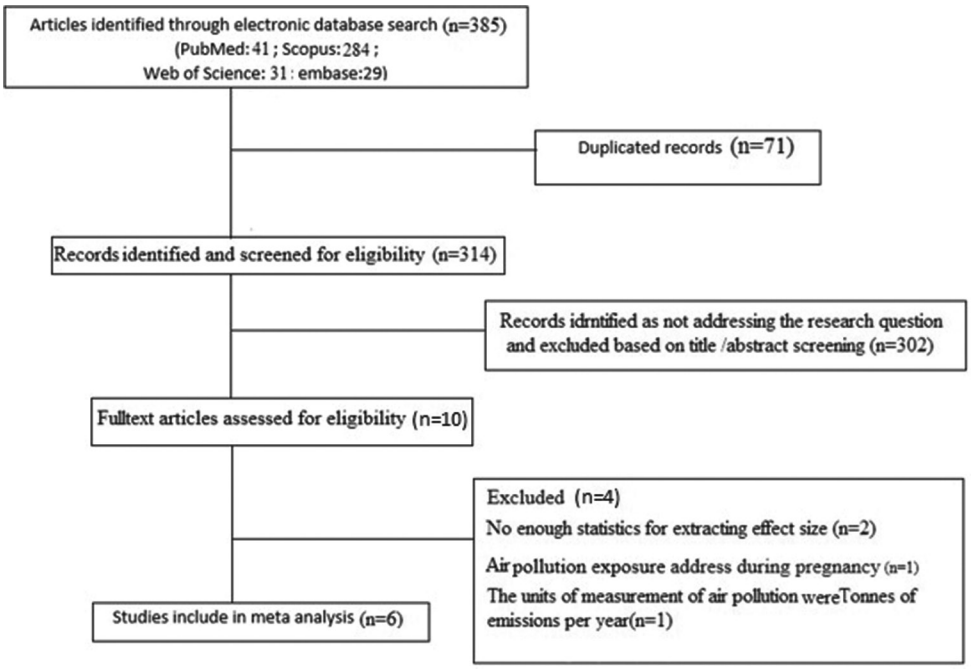

Figure 1: Flow diagram of study selection process

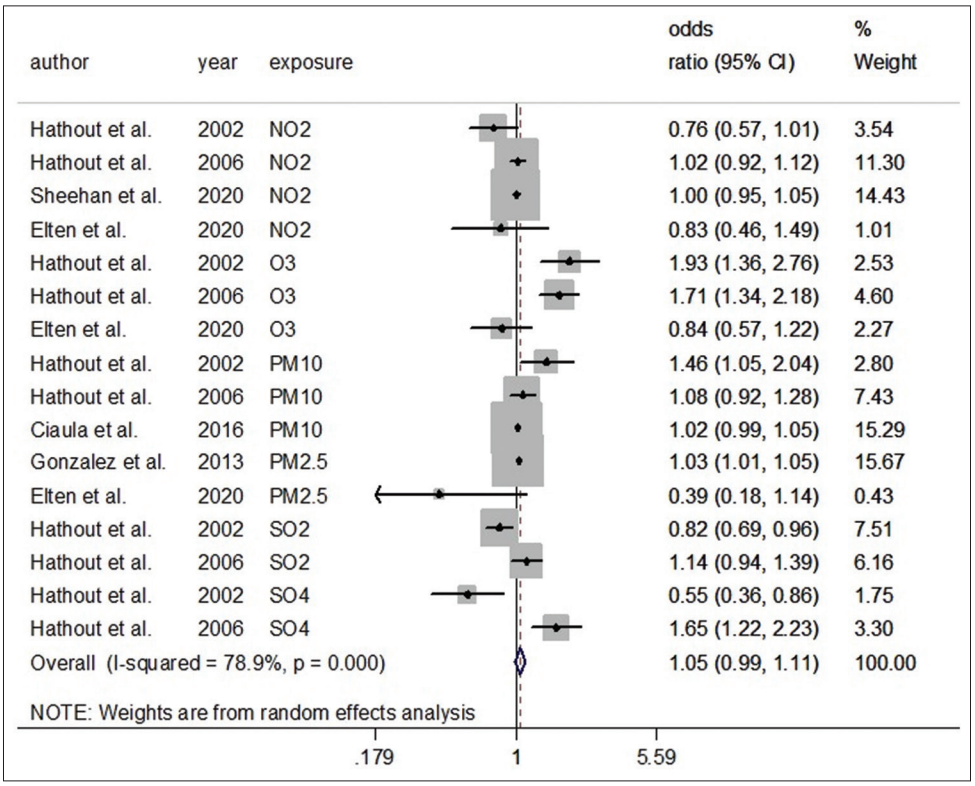

Figure 2: Forest plot for the association of exposure to air pollution and type 1 diabetes mellitus (random effect model)

Discussion

Studies on the association between air pollution exposure and T1DM are rare and results are inconsistent. This study assessed the link between exposure to air pollutants (O_3, PM_{10}, $PM_{2.5}$, SO_4, SO_2, and NO_2) and the risk of T1DM. This systematic review and meta-analysis showed a positive association between exposure to ozone and $PM_{2.5}$ and the risk of T1DM in children and adolescents. However, the overall association between T1DM and higher exposures to PM_{10}, SO_4, SO_2, and NO_2 was not statistically significant.

Table 1: Summaries of studies included in the systematic review

Author/date	Type of study (year)	Location	Number of participants	Gender, age (years)	Matching and adjustment factors	Exposure	Effect size (95% CI)
Di Ciaula[24]	Population-based study (2016)	Apulia, Italy	631,275 (1501 T1DM case)	Male/female, 0-14	Aggregate data over 13 years 2001-2013, adjusted for age group, gender, year of diagnosis and other pollutants (NOx, CO, ozone)	PM_{10} (µg/m^3)	OR: Tertile 1: Ref Tertile 2: 1.018 (0.986-1.051) Tertile 3: 1.037 (1.0021.07)
González *et al.*[25]	Population-based study (2013)	Santiago, Chile	Very large, (total number of T1DM cases not provided)	Male/female, 0-15	Aggregate weekly data over 7 years (period 2000-2007), not adjusted for individual patient characteristics RR: per 1 - µg/m^3 increase Coefficient of β	$PM_{2.5}$	RR=1.003 (1.001-1.005) β=0.003116 SE=0.00104
Di Ciaula[14]	Population-based study (2014)	16, European countries	Very large, (total number of T1DM cases not provided)	Male/female, 0-15	Aggregate nation-wide data over 20 years (1990-2010); not adjusted for individual patient characteristics	PM_{10}	OR: Tertile 1: Ref Tertile 2: 1.069 (0.921-1.23) Tertile 3: 1.24 (1.051.46)
						NOx	OR: Tertile 1: Ref Tertile 2: 1.08 (0.941.24) Tertile 3: 1.20 (1.03-1.39)
						VOCs	OR: Tertile 1: Ref Tertile 2: 1.033 (0.91-1.183) Tertile 3: 1.20 (1.031.38)
						SOx	OR=1.16 (1.2-1.3)
						Ammonia	OR=1.15 (1.0-1.3)
Hathout *et al.*[15]	Casecontrol (2006)	Loma Linda, California	402 children (102 T1DM case)	Male/female, age 0-17	Adjusted variables were not reported OR: Per 10- µg/m^3 increase NO_2, O_3, PM_{10}, SO_4 and for a 1 - µg/m^3 increase in SO_2	Ozone (ppb)	OR=2.89 (1.86-4.58)
						NO_2 (ppb)	OR=1.03 (0.71-1.50)
						PM_{10} (µg/m^3)	OR=1.08 (0.87-1.34)
						SO_2 (ppb)	OR=1.42 (0.91-2.21)
						SO_4 (µg/m^3)	OR=1.65 (1.20-2.28)
Hathout *et al.*[16]	Case control study (2002)	California, USA	100 children (61 case)	Male/female, under and over 5 year	Adjusted for age group OR: Per IQR increase Coefficient of β	Ozone (ppb)	OR=4.22 (1.96-9.10) IQR=10.9
						PM_{10} (µg/m^3)	OR=2.37 (1.11-5.03) IQR=22.65
						SO_2 (ppb)	OR=0.52 (1.31-0.88) IQR=1.235
						NO_2 (ppb)	OR=0.56 (0.30-1.03) IQR=11.175
						SO_4 (µg/m^3)	OR=0.55 (0.35-0.85) IQR=1.025
Elten *et al.*[26]	Retrospective population-based cohort study, (2020)	Ontario, Canada	754,698 children (1094 case)	Male/female, 0-5 years	Adjusted for exposures to the selected pollutant during pregnancy, maternal age at delivery, infant sex, parity, maternal smoking during pregnancy, gestational age, birth weight, residential greenness exposure during pregnancy, maternal diabetes, maternal preeclampsia, season of conception and family income	$PM_{2.5}$ (µg/m^3)	HR=0.70 (0.52-1.05) IQR (in µg/m^3)=3.80
						NO_2 (ppb)	HR=0.79 (0.38-1.64) IQR (ppb)=6.56
						Ozone (ppb)	HR=0.89 (0.69-1.14) IQR (ppb)=3.31
						Ox (ppb)	HR=0.58 (0.24-1.14) IQR (ppb)=5.00
Sheehan *et al.*[27]	An environment wide association study	England	13,948 cases of type 1 diabetes	Male/female, 0-9 years	Adjusted for age and sex OR: Per 1 - µg/m^{3}increase NO_2	NO_2 (µg/m^3)	RR=1 (0.995-1.005)

SE: Standard error, CI: Confidence interval, IQR: Interquartile range, HR: Hazard ratio, OR: Odds ratio, RR: Relative risk, T1DM: Type 1 diabetes mellitus, PM_{10}: Particulate matter <10 µm, NOx: Nitrogen oxides, VOCs: Volatile organic compounds, NO_2: Nitrogen dioxide, O_3: Ozone, SO_4: Sulfate, SO_2: Sulfur dioxide, $PM_{2.5}$: Fine particulate matter

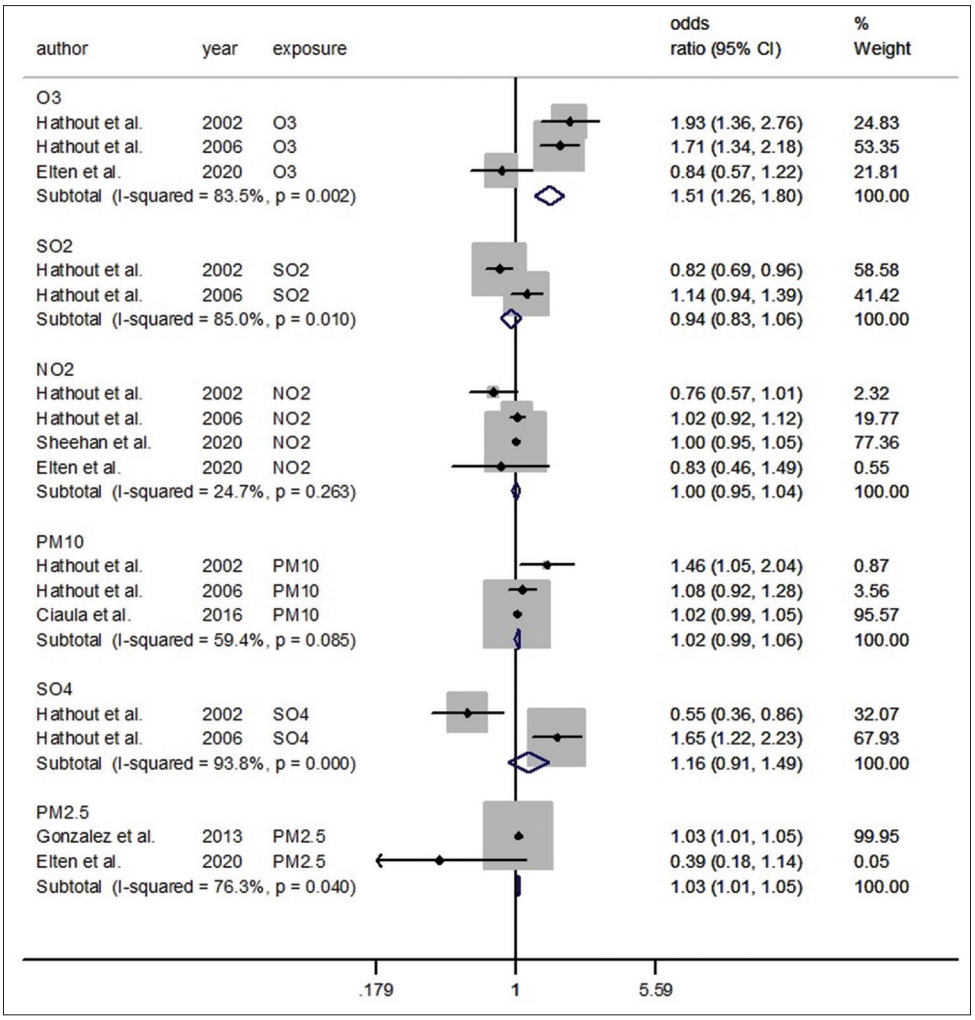

Figure 3: Forest plot of the association between air pollution and type 1 diabetes mellitus regarding each pollutant (fixed effect model)

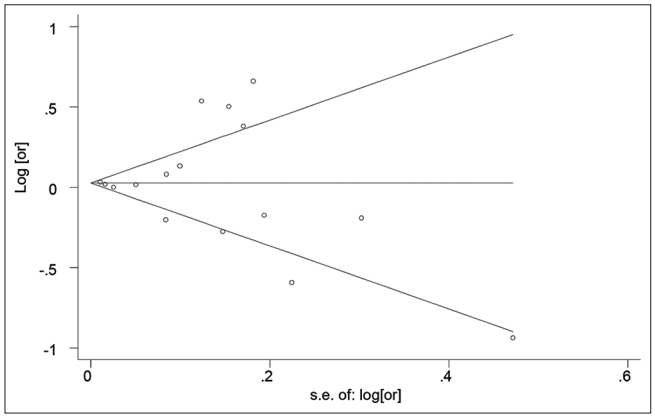

Figure 4: Funnel plot for the effects of air pollution and type 1 diabetes mellitus

Our results revealed a link between O_3 exposure and increased risk of T1DM. The interaction of NOx, hydrocarbons, and ultraviolet energy led to O_3 production. Ozone can oxidation or peroxidation of biomolecules directly or indirectly (free radical reactions).[16,28,29] The biological mechanism through which O_3 exposure can increase the prevalence of T1DM is complex and not fully understood. O_3 exposure creates the free oxygen radicals that can cause damage to βcells or increase the presentation of diabetogenic antigens and resulted in predisposing to T1DM. Ozone can make an internal milieu that is typical of autoimmune diseases such as T1DM with altering T-cell and affecting $CD4^+$ cells.[30] The presence of certain diabetogenic antigens in children that occurred because of the immature pulmonary or ambient air barriers may be elevated due to the synergism effect of ozone in case of simultaneous presence with sulfate in ambient.[31] A case–control study among 402 children aged 0–17 years showed that exposure to O_3 and sulfate in ambient air may predispose to the development of T1DM. Hathout *et al*. found that ozone exposure has a strong positive association withT1DM.[16] However, some recent studies indicated that levels of O_3 were not significantly associated with T1DM incidence in children.[24]

Findings of this review indicated that there was no evidence of the association between increased risk of T1DM and exposure to NO_2, SO_2, and PM_{10} levels. In 2020, a retrospective cohort study by Elten *et al*. in Ontario, Canada showed that exposure

Table 2: Pooled effect sizes and between study heterogeneity stratified by gaseous and particulate air pollutants

Exposure	Number of studies	Random effect Effect size		Heterogeneity		Fixed effect Effect size
		Pooled OR (95% CI)	I^2 (%)	Q ($P_{heterogeneity}$)	T^2	Pooled OR (95% CI)
Total	16	1.05 (0.99-1.11)	78.9	71.19 (<0.001)	0.006	1.03 (1.01-1.04)
PM_{10}	3	1.09 (0.95-1.25)	59.4	4.93 (0.08)	0.009	1.02 (0.99-1.06)
$PM_{2.5}$	2	0.71 (0.28-1.79)	76.3	4.22 (0.04)	0.360	1.03 (1.01-1.05)
O_3	3	1.42 (0.89-2.25)	83.5	12.09 (0.002)	0.140	1.51 (1.26-1.80)
SO_4	2	0.97 (0.33-2.83)	93.8	16.17 (<0.001)	0.560	1.16 (0.91-1.49)
SO_2	2	0.96 (0.69-1.34)	85.0	6.67 (0.0.01)	0.050	0.94 (0.83-1.06)
NO_2	4	0.99 (0.92-1.06)	24.7	3.98 (0.26)	0.001	1.00 (0.95-1.04)

T^2: Estimation of between-studies variance, OR: Odds ratio, CI: Confidence interval, PM_{10}: Particulate matter <10 μm, O_3: Ozone, SO_4: Sulfate, SO_2: Sulfur dioxide, NO_2: Nitrogen dioxide, $PM_{2.5}$: Fine particulate matter

to air pollution (O_3, NO2, $PM_{2.5}$) during childhood was not associated with pediatric diabetes incidence.[26]

There are also some evidence regarding prenatal exposure to pollutants and the development of T1DM in offsprings. The positive association between prenatal exposures to NOx and O_3 with increased risks of developing T1DM was reported by Malmqvist *et al*.[13]

Few studies have investigated the relation between air pollution and T1DM in children and adolescents. For instance, a population-based study from southern Italy on 0-to 14-year-old children showed a positive relationship between levels of PM_{10} and T1DM incidence.[24] Similarly, a study from 16 European Countries (1990-2010) among children aged 0–15 years found positive associations between nationwide emissions of PM_{10}, NO_x, and VOCs and T1DM incidence.[14] Moreover, González *et al*. in a population-based study (2013) on children aged less than 15 years in Chile from 2000 to 2007, found that (PM_{10}, PPM $_{2.5,}$ is associated with T1DM incidence.[25] Results of a study among children and adolescents, in Poland by Michalska *et al*. revealed that mean annual PM_{10} concentration was positively associated with T1DM incidence in 2016, but not in the year 2015.[22] In 2020, Michalska *et al*. in Poland showed that high exposure to PM_{10}, SO_2, and CO related to the risk of developing T1DM in children, however, NO_2 and NO were not found associated with the risk of developing T1DM.[23] Using an ecological regression model, Sheehan *et al*. showed that nitrogen dioxide was not associated with T1DM risk in children in England.[27] The exact mechanisms linking air pollution to T1DM are not fully understood. Some possible mechanisms have been introduced in this field. Both *in vivo* and *in vitro* studies demonstrated that exposure to pollutant particles even for short time could trigger inflammatory reactions.[32,33] Some evidence indicated that exposure to PM results in the formation of reactive oxygen species in pulmonary endothelial cells and circulating monocytes, which consequently result in DNA damage and activation of inflammatory reactions.[23,34,35]

A multicenter observational study conducted by Puett *et al*., 2019, on 2566 participants showed that $PM_{2.5}$ exposures were associated with indicators of inflammation, interleukin-6 levels, after adjusting for demographic and lifestyle variables among youth.[36] A recent systematic reviews and meta-analyses showed that elevated fasting blood glucose was associated with exposure to both PM_{10} and $PM_{2.5}$.[37] However, a cross-sectional study conducted by Tamayo *et al*. in Germany showed that exposure to PM_{10} and NO_2 were not associated with glycemic control in children and young adults with T1DM.[17]

The main limitation of this study was the limited number of included studies. Furthermore, most published studies were from European and American countries; limited studies are available for other countries. Given the limited evidence, further prospective studies should be conducted to verify the effect of air pollutants on the risk of T1DM in children, particularly from developing countries. Another limitation was the considerable heterogeneity among the studies. The heterogeneity is likely to be related to different exposure assessment methods, study design, and other uncontrolled confounders in the studies included in the meta-analysis.

Considering the limited number of included studies, we conducted fixed-effect model meta-analysis.

The methods of measuring air pollution concentration were not uniform. In some studies, the concentrations of air pollutants were estimated from fixed-site monitoring stations to zip code centroids which are more accurate scale,[15,16] but some studies estimated air pollution exposure through citywide air pollution exposure levels.[24]

Given that, T1DM in the pediatric age group is affected by multiple factors. Some studies did not adjust for individual patient characteristics, which may affect the study results.

Together, they illustrate that the role of chemicals in T1DM may be complex and may depend on a variety of factors, such as exposure level, the timing of exposure, nutritional status, and chemical metabolism.[38]

Conclusions

This systematic review and meta-analysis indicated a positive association between $PM_{2.5}$ and O_3 exposure with the increased risk of T1DM in children and adolescents. While the evidence that these exposures may increase the risk of T1DM is still

preliminary, it is critical to investigate this possibility further as a means of preventing T1DM.

Interventions and prevention programs should be considered to reduce exposure to air pollution and its adverse health effects in children and adolescents by health policymakers.

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Conflicts of interest

There are no conflicts of interest.

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