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Meta-Analysis

Investigating the Association Between Traffic-related Air Pollution (PM2.5 and Benzene) and the Risk of Asthma: A Systematic Review and Meta-analysis

Maryam Nazari[1], Abdollah Mohammadian-Hafshejani[2], Mohsen Arbabi[1*]

[1]Department of Environmental Health Engineering, School of Health, Shahrekord University of Medical Sciences, Shahrekord, Iran
[2]Department of Epidemiology and Biostatistics, School of Health, Modeling in Health Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran

Abstract

Background and aims: Asthma is a chronic disease that causes respiratory system inflammation. Recently, traffic-related air pollution (TRAP), especially particulate matter ($PM_{2.5}$) and benzene, has been considered a factor that may increase the risk of asthma. This study investigated the association between TRAP ($PM_{2.5}$ and benzene) and asthma risk.

Methods: In this systematic review and meta-analysis, the relevant published data were collected by searching the Cochrane Library, Web of Science, ScienceDirect, Scopus, PubMed, and Google Scholar databases up to November 2022. The study quality was evaluated using the Newcastle-Ottawa Scale checklist. The data were analyzed using Stata software (version 14), and the significance level in this meta-analysis study was considered to be < 0.05.

Results: In the first search, 4,909 and 4,825 studies were extracted for $PM_{2.5}$ and benzene, respectively. After evaluating and considering the search criteria, 25 and 4 studies remained for $PM_{2.5}$ and benzene, respectively. For $PM_{2.5}$, the odds ratio (OR) for developing asthma in the TRAP-exposed group compared to the unexposed group was 1.11 (95% confidence interval [CI]: 1.04-1.19, $P = 0.002$). For benzene, the OR of developing asthma in the exposed group was 1.19 when compared to the unexposed group (95% CI: 1.10-1.29, $P < 0.001$).

Conclusion: Based on this review study, there was a positive association between TRAP exposure and the development of asthma. The results confirmed that $PM_{2.5}$ and benzene increase the risk of asthma.

Keywords: Asthma, Air pollution, Benzene, Particulate matter, Traffic-related pollution

***Corresponding Author:**
Mohsen Arbabi,
Email: marbabi47@yahoo.com

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Introduction

Asthma, a chronic condition characterized by inflammation and narrowing of the airways, results in symptoms such as coughing, wheezing, and difficulty breathing.[1-3] These symptoms can change in severity and frequency over time and may occur alongside fluctuating restrictions in expiratory airflow.[1] Prevalence rates vary, with studies indicating a range of 15%–20% across different countries, particularly in developed nations.[2] Triggers for asthma exacerbations include viral infections, environmental pollutants, and lifestyle factors such as obesity.[4-6] Environmental factors, especially air pollution, are increasingly recognized as significant contributors to asthma development.[7,8] Traffic-related air pollution (TRAP) is a primary source of urban air pollutants, including particulate matter ($PM_{2.5}$), ozone, and benzene, which are closely linked to vehicle emissions and strongly impact health.[9,10] Research on the relationship between TRAP and asthma has yielded inconsistent results. Some studies have found a strong positive association between $PM_{2.5}$ exposure and increased asthma exacerbations and hospitalizations.[11,12] Similarly, benzene exposure has been linked to increased asthma symptoms and emergency room visits.[13,14] However, other studies have failed to establish a significant correlation, suggesting a complex relationship influenced by various confounding factors.[15,16] The inconsistencies in findings may be due to differences in study designs, exposure assessment methods, and the populations studied.[17,18] Factors such as personal exposure monitors versus fixed monitors, age, socioeconomic status, and underlying health conditions may influence the association between TRAP and asthma.[19,20] Additionally, other environmental factors, such as indoor air pollution and allergens, may modify the impact of TRAP on asthma.[21,22] The mechanisms through which TRAP contributes to asthma are not fully understood but involve pathways such as inflammation, oxidative stress, and airway hyperreactivity.[23-26] Given the controversy surrounding the role of TRAP in asthma, this study aims to investigate the association between TRAP, particularly $PM_{2.5}$ and benzene, and asthma risk through a systematic review and meta-analysis. By synthesizing evidence from various studies, it is attempted to clarify the contribution of TRAP to asthma and inform public health policies to reduce the burden of this chronic respiratory disease. In summary, the existing literature on the association between TRAP and asthma needs to be more consistent, highlighting the need for a comprehensive review of the evidence. This study seeks to fill this gap by conducting a systematic review and meta-analysis of the available studies on the association between $PM_{2.5}$ and benzene exposure from traffic and asthma risk. This approach will contribute to a better understanding of the role of TRAP in asthma and support future research and policy decisions.

Materials and Methods

Study Design

This research comprises a comprehensive literature review and statistical synthesis to examine the relationship between TRAP and asthma risk by analyzing data from observational studies up to November 2022. The MOOSE guidelines were followed in this observational systematic review and meta-analysis.

The PICO framework [P (population), I (intervention), C (comparison), O (outcome)] is a widely used tool in evidence-based practice, especially in the context of systematic reviews and meta-analyses.

Search Strategies

Databases of Cochrane Library, Web of Science, ScienceDirect, Scopus, PubMed, and Google Scholar were used for a comprehensive literature search and data collection. In this study, $PM_{2.5}$ and benzene were considered exposure variables, and asthma risk was regarded as the outcome. The data search was performed using several keywords such as “air pollution”, “$PM_{2.5}$”, “inorganic”, “traffic”, and “asthma” using the operators AND, OR, and the associated synonyms based on Medical Subject Headings (MeSH). The data search was also performed using the keywords “air pollution”, “benzene”, “organic”, “traffic, “asthma”, and associated synonyms based on MeSH.

Inclusion and Exclusion Criteria

No restrictions were placed on study quality, time, or location. All English-language research studies (case-control, cohort, and cross-sectional studies) about the association between TRAP and asthma risk were entered into the study. On the other hand, conference studies, review studies, letters to the editor, case reports, and studies without full-text availability were excluded from the study.

Study Selection and Data Extraction

All retrieved articles were entered into the EndNote software (version 8). Duplicate studies were deleted using the endnote software. Unrelated studies were also deleted after checking the titles, abstracts, and full texts. For each study, two researchers extracted the information independently, and a third researcher resolved any differences found in the assessment of the studies. For studies that were not accessible, the authors requested the full text of the studies by email.

Quality Assessment

The Newcastle-Ottawa Scale (NOS) checklist for case-control, cohort, and cross-sectional studies supplemented the list for the quality assessment of studies. This scale evaluates non-randomized studies based on three key domains, namely, selection of study groups, comparability between groups, and ascertainment of exposure and outcome variables. Based on the NOS, studies are scored from zero (the weakest study) to 9 (the most robust study). This tool divides the studies into low, medium, and high categories, depending on the type of study and the corresponding checklist.

Data Analysis

In the present study, the value of the odds ratio (OR), or relative risk (RR), and the 95% CI were extracted and used since the statistical analyses were based on the OR or RR. Statistical and graphical tests were used to check for heterogeneity or lack of uniformity among the research papers incorporated in the statistical synthesis. Statistical heterogeneity was also assessed using the Q-test or I^2. The forest plot is utilized to evaluate heterogeneity graphically. The chi-square test was employed to check the differences between the results. The funnel plot, Egger’s regression test, and Begg’s adjusted rank correlation test were used to assess publication bias. All analyses were performed using Stata software (version 14), and the significance level in this meta-analysis study was < 0.05.

Results

Assessment of the Association of $PM_{2.5}$ and the Development of Asthma

Through an electronic search in databases using the intended keywords (air pollution, $PM_{2.5}$, inorganic, traffic, asthma) and their synonyms in MeSH, regardless of the time limit, 4,909 published studies were collected until November 2022. The studies were managed and evaluated using EndNote software. After removing duplicates, 4,110 studies remained. After considering the study titles, 3,720 studies were removed, and 390 studies remained. After reviewing the abstracts of the remaining studies, 179 studies were removed and 211 studies remained. Based on the topic and the inclusion and exclusion criteria, 186 studies were removed (163 studies were excluded because the full text was not relevant, 13 studies were excluded based on conference abstracts, and ten studies were excluded because the full text was not accessible). Finally, 25 studies underwent analysis (Figure 1).

Of the 25 studies analyzed in the meta-analysis, 22 were cohort studies; two employed a cross-sectional design, while one utilized a case-control approach. Among these studies, 13 were conducted in Europe, nine were performed

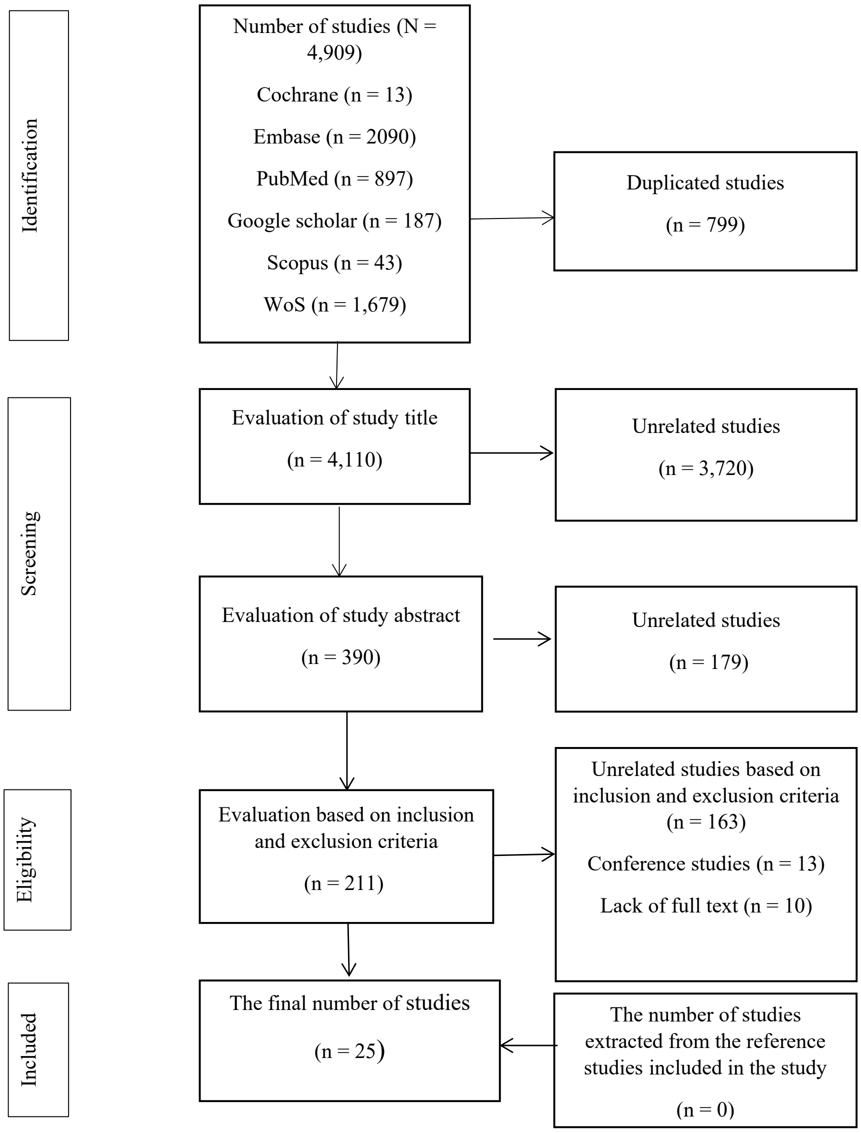

Figure 1. Diagram Showing the Flow of Chosen Research for the Meta-analysis Evaluating the Connection Between Asthma and $PM_{2.5}$

in America and Canada, two were conducted in Asia, and one was performed in Australia. The total population examined in these studies was 1 525 507. The information on the studies is summarized in Tables 1 and 2.

The assessment of the association between exposure to TRAP and the development of asthma based on the results of 25 studies in the meta-analysis revealed that the OR for the development of asthma was 1.11 (95% CI: 1.04-1.19; $P=0.002$) in the group exposed to TRAP compared to the unexposed group. This meta-analysis showed that the likelihood of developing asthma increased by 11% compared to the control group. This difference was considered statistically significant (Figure 2).

Assessment of Publication Bias

The Egger test ($P=0.978$) and the Begg test ($P=0.018$) were performed to assess possible publication bias in the reported studies (Figure 3).

The Begg test results indicated publication bias, suggesting that published research on the correlation linking TRAP exposure to asthma onset is significantly influenced by such bias. This could affect the overall results of the meta-analysis. The effect size was estimated for potentially missing studies using the trim and fill method. Figure 4 illustrates this method, which estimated the results for nine missing studies. Considering these missing studies, the revised OR was 1.03 (95% CI: 0.95-1.11, $P=0.445$).

Meta-regression Analysis

In this meta-analysis, the heterogeneity between the results of the studies was 94.9%. A meta-regression analysis was conducted to explore the sources of heterogeneity among the results of different studies examining the association between TRAP and the risk of developing asthma, incorporating variables such as publication year, geographic location, sample size, study design, average age, and quality assessment score. The results of the meta-regression analysis revealed no statistically significant sources of heterogenicity ($P>0.05$), indicating that these elements were not responsible for the detected variability in results.

Table 1. Features of the Studies to Explore the Connection Between Air Pollution From Traffic ($PM_{2.5}$) and the Likelihood of Developing Asthma

First Author	Year	Study Design	Diagnosis Method	Study Setting	Average Age (y)	Exposure Assessment	Sample Size	OR	95% CI	Quality Score
Brauer[27]	2002	†	§	The Netherlands	2	LUR model	2,989	1.12	0.84-1.5	8
Brauer[28]	2007	†	§	The Netherlands	4	LUR model	2,826	1.32	0.96-1.83	7
Clark[29]	2010	†	§	Canada	4	LUR model	37,401	1.01	0.99-1.03	9
Fuertes[30]	2013	†	§	Germany	6.5	LUR model	4,585	0.97	0.59-1.58	8
Gehring[31]	2002	†	§	Germany	2	LUR model	1,756	0.92	0.78-1.09	8
Gehring[32]	2010	†	§	The Netherlands	8	LUR model	3,143	1.26	0.97-1.63	7
Gehring[33]	2015	†	§	The Netherlands	15	LUR model	14,126	1.25	0.94-1.66	7
Morgenstern[34]	2008	†	§	Germany	5	Monitoring data	2,436	1.56	1.03-2.37	6
Molter[35]	2014	†	§	England	9	LUR model	10,377	1.23	0.78-1.95	7
Tereault[36]	2016	†	§	Canada	12	LUR model; satellite imagery	1,133,938	1.31	1.28-1.33	8
Wang[37]	2015	†	∆	Taiwan	5.5	Monitoring data	2,661	1.45	1.07-1.97	6
Yang[38]	2016	†	§	The Netherlands	14	LUR model	3,701	1.02	0.87-1.18	9
Nishmura[39]	2013	*	§	USA	14.5	Monitoring data	3,015	1.02	0.93-1.12	9
Abidin[40]	2014	‡	§	Malaysia	11	Monitoring data	1,952	1.15	0.49-2.73	7
Rice[41]	2015	†	§	USA	50.4	Distance to the main road	2,783	0.97	0.85-1.10	9
Khreis[42]	2018	†	§	USA	9	LUR model	9,804	1.03	1.01-1.05	9
Young[43]	2014	†	§	USA	55.1	LUR model	35,862	1.2	0.99-1.46	6
Gehring[44]	2020	†	∆	The Netherlands	10	LUR model	3,191	1.19	1.04-1.36	7
Hales[45]	2021	†	§	New Zealand	11	Monitoring data	11,139	1.03	0.89-1.18	8
Liu[46]	2021	†	§	Denmark	52.2	Monitoring data	23,093	1	0.74-1.35	9
Liu[47]	2021	†	§	Denmark	55.4	LUR model	98,326	1.22	1.04-1.43	8
Annesi-Maesano[48]	2007	†	∆	France	10.4	Monitoring data	5,338	1.04	0.85-1.28	8
Schultz[49]	2017	†	§	USA	47.5	Monitoring data	3,375	1.51	1.14-2	7
Sinclair[50]	2014	†	§	USA	7.05	Monitoring data	11,049	1.02	0.94-1.10	8
Kim[51]	2004	‡	∆	USA	10.5	Monitoring data	96,641	1.04	0.96-1.12	9

Note. OR: Odds ratio; CI: Confidence interval.
†Cohort.
‡Cross-sectional.
*Case-control.
§Doctor-diagnosed.
∆Questionnaire.

Sensitivity Analysis

In addition to meta-regression, a sensitivity analysis approach was used to identify the source of heterogeneity (Figure 5). This method is utilized to determine each study's impact on the analysis's outcome. In this method, the final effect is estimated by removing one study at a time to assess the reliability of the results of the meta-analysis. This analysis represented that the estimated OR was not affected by any of the included studies, demonstrating the strength of the meta-analysis results.

Subgroup Analysis

Subgroup analysis was performed based on study type, geographic location, sample size, mean age, and study year. It was found that the OR in cohort, cross-sectional, and case-control studies was 1.13 (95% CI: 1.05-1.21, $P<0.001$), 1.04 (95% CI: 0.96-1.12, $P=0.819$), and 1.02 (95% CI: 0.93-1.12, $P=0.265$), respectively. In studies conducted in 2014 (and before this year) and 2015 (and after this year), the OR was 1.03 (95% CI: 1.00-1.06, $P=0.078$) and 1.15 (95% CI: 1.03-1.28, $P=0.012$), respectively. The OR in studies with a sample size of less than 5,000 and more than 5,000 people was 1.12 (95% CI: 1.03-1.22, $P=0.010$) and 1.10 (95% CI: 1.00-1.20, $P=0.041$), respectively. The OR in the studies based on location was 1.09 (95% CI: 0.99-1.20, $P=0.079$) in America and Canada, 1.12 (95% CI: 1.04-1.20, $P=0.002$) in Europe, 1.41 (95% CI: 1.06-1.88, $P=0.019$) in Asian countries, and 1.03 (95% CI: 0.89-1.19, $P=0.681$) in Australia and New Zealand. In studies with a mean age of less than ten years and more than ten years, the OR was 1.04 (95% CI: 1.01-1.08, $P=0.024$) and 1.12 (95% CI: 1.01-1.23, $P=0.027$), respectively.

Assessment of the Association of Benzene and the Development of Asthma

By searching databases with specific keywords (air pollution, benzene, organic, traffic, and asthma) and their synonyms in MeSH, regardless of the time limit, 4825 published studies were found by November 2022. The studies were managed and evaluated using EndNote

Table 2. Adjusted Variables to Determine the Association Between TRAP ($PM_{2.5}$) and the Risk of Developing Asthma

Authors	Year	Adjusted Variables
Brauer et al[27]	2002	Tobacco use, the intervention group/mattress protector, level of education, gender, and other factors
Brauer et al[28]	2007	Tobacco use, the intervention group/mattress protector, level of education, gender, and other factors
Clark et al[29]	2010	Equality, breastfeeding, socioeconomic status (based on the neighborhood), educational attainment of mothers (based on the neighborhood), infant's birth weight, and pregnancy duration
Fuertes et al[30]	2013	Gender, age, family history of allergies, parental level of education, presence of older siblings, maternal smoking while pregnant, exposure to secondhand smoke at home, interaction with pets, gas stove for cooking, and presence of indoor mold at home
Gehring et al[31]	2002	Gender, parental history of allergies (yes/no), maternal level of education, presence of siblings (yes/no), exposure to secondhand smoke at home, home environment, and gas for cooking
Gehring et al[32]	2010	Attending daycare, smoking habits, type of intervention received (e.g., mattress cover), level of education, gender, and other relevant factors
Gehring et al[33]	2015	The factors include a history of asthma and hay fever in the mother and father, the family's nationality, the parents' level of education, whether the child was breastfed, the presence of older siblings, smoking by parents at home, daycare attendance, smoking during pregnancy, the presence of mold at home, ownership of pets, and cooking gas
Morgenstern et al[34]	2008	Gender, age, family history of allergies, mother's level of education, number of siblings, exposure to secondhand smoke at home, cooking with gas, presence of mold at home, and ownership of pets
Molter et al[35]	2014	Gender, presence of older siblings, age, using gas cooking, > 12 weeks of breastfeeding, mold, smoker living at home, maternal age at birth, smoking during pregnancy, dog ownership, attending daycare, parental atopic, personal socioeconomic status, and cat ownership
Tereault et al[36]	2016	Date of birth, gender, indicators of social and economic disadvantage
Wang et al[37]	2015	Age, gender, BMI, exposure to secondhand smoke, family history of allergies, number of siblings, mother's level of education and country of origin, temperature, length of breastfeeding, amount of sleep, humidity, and proximity to an air quality monitoring site
Yang et al[38]	2016	Gender, maternal education, pets at home, parental allergies, smoking habits, gas for cooking, smoking during pregnancy, mold in the child's home, breastfeeding, daycare during the first year, and neighborhood low-income households
Nishimura et al[39]	2013	Gender, age, location, race, combined economic status, family's asthma, exposure to secondhand smoke, smoking during pregnancy, and the like
Abidin et al[40]	2014	Geographical area, individual's gender, parental history of asthma, the highest level of parental education, household income, secondhand smoke exposure within the household, rules regarding smoking indoors, daily duration of exposure to secondhand smoke, recent installation of carpeting and furnishings in the child's room and throughout the home within the past year, presence of mold, ventilation systems at home, ownership of pets, and use of mosquito repellent coils
Rice et al[41]	2015	Age, gender, height, body mass, pack-year smoking history, socioeconomic status markers, study group, timeframe, seasonal variations, and atmospheric conditions
Khreis et al[42]	2018	-
Young et al[43]	2014	Age, BMI, ethnicity, education level, exposure to vapors or fumes at work, exposure to dust at work, smoking history, age of smoking initiation, daily cigarette consumption, continuous smoking since baseline, childhood exposure to second-hand smoke, access to healthcare, and daily intake of dietary fiber are all considered in the study
Gehring et al[44]	2020	Gender, breastfeeding, age, paternal asthma, smoking during pregnancy, highest level of parental education, attending daycare, Dutch nationality, household smoking habits, dampness at home, active smoking (from age 14 years), hay fever, pets, and cooking gas
Hales et al[45]	2021	Age, gender, ethnicity, personal income, education, smoking, and temperature
Liu et al[46]	2021	Physical activity level, smoking habits, BMI, avoiding fatty meat, occupational status, marital status, alcohol consumption, NO_2, and vegetable consumption
Liu et al[47]	2021	At the municipality level in 2001, the area-level mean income for the Danish Diet, Cancer and Health and Danish Nurse Cohort studies, and neighborhood-level data from 1994 for the Cardiovascular Effects of Air Pollution and Noise in Stockholm study
Annesi-Maesano et al[48]	2007	Age, gender, family history of allergy, and passive smoking
Schultz et al[49]	2017	Gender, age, BMI, smoking status, education, and income
Sinclair et al[50]	2014	-
Kim et al[51]	2004	Pests, an indicator of mold presence, a child's respiratory illness before age 2, and a mother's history of asthma

Note. TRAP: Traffic-related air pollution; PM: Particulate matter; BMI: Body mass index.

software. After removing duplicates, 4057 studies remained. After assessing the titles of the studies, 3675 studies were removed, and 382 studies remained. After reviewing the abstracts of the remaining studies, 362 studies were removed and 20 studies remained. After assessing the remaining studies, 10, 3, and 3 were removed because the full text was irrelevant, the conference abstract needed to be more relevant, and there needed to be access

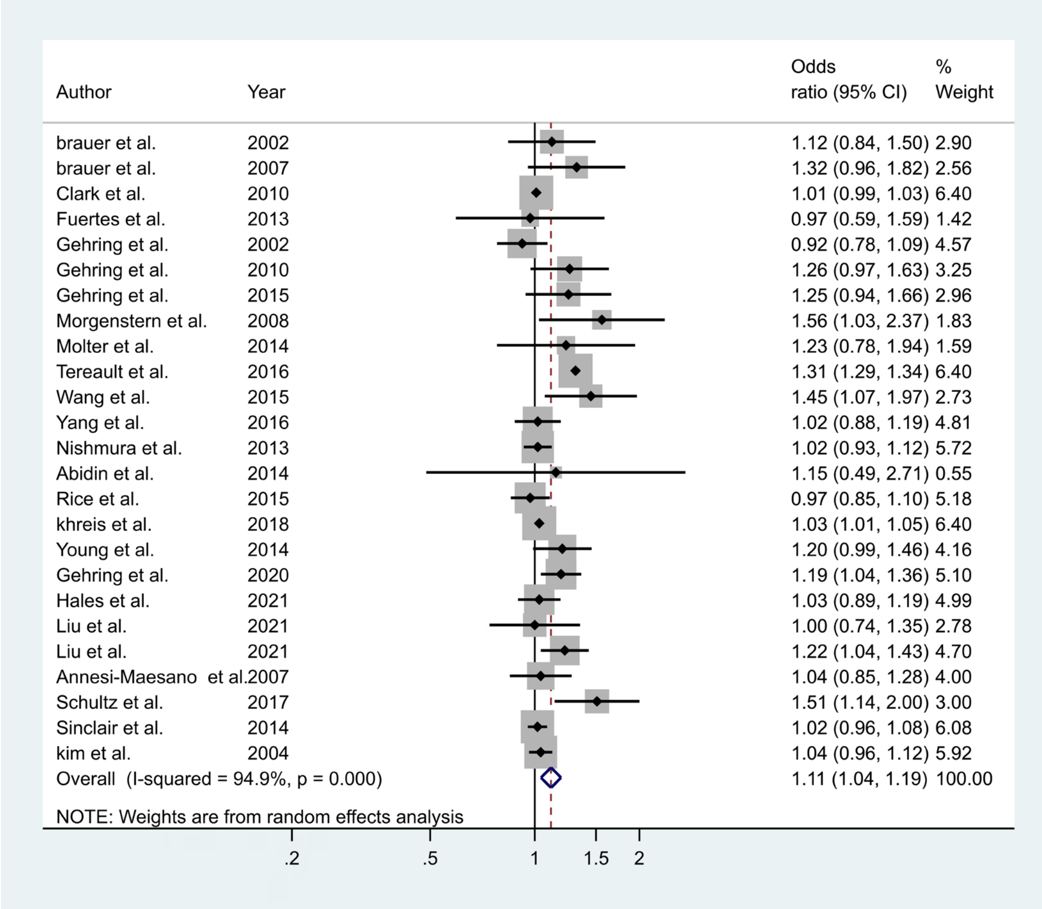

Figure 2. The Association Between TRAP ($PM_{2.5}$) and the Risk of Asthma. *Note*. CI: Confidence interval; TRAP: Traffic-related air pollution; PM: Particulate matter

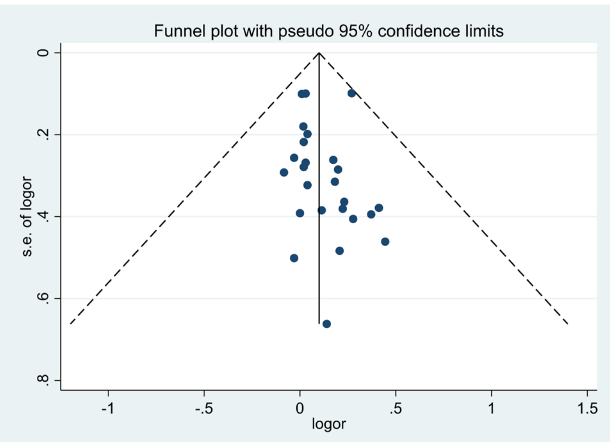

Figure 3. Assessment of Publication Bias in Meta-analytical Research on the Association Between Asthma Risk and TRAP ($PM_{2.5}$). *Note*. TRAP: Traffic-related air pollution; PM: Particulate matter

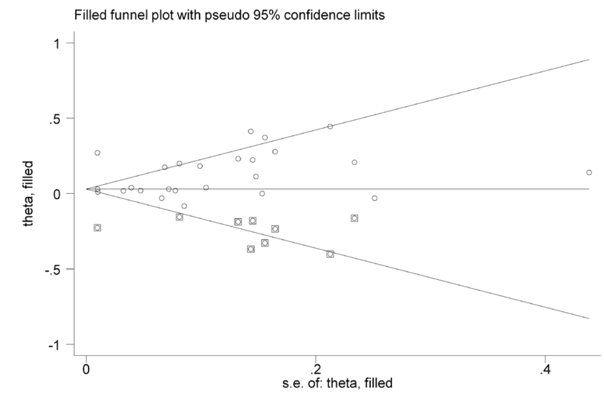

Figure 4. Calculating the Effect Size Amount in the Studies That Are Lacking

to the full text. Finally, four studies remained for analysis. Among these four studies, a single investigation employed a longitudinal design, while a trio of studies utilized cross-sectional methodologies. One study was conducted in America, two studies were performed in Germany, and one study was conducted in France. The population examined in these studies comprised 31 094 people (Figure 6).

Tables 3 and 4 provide the information on the studies.

The evaluation of the relationship linking TRAP exposure to asthma onset showed that the OR for the development of asthma in the exposed group compared to the unexposed group was 1.19 (95% CI: 1.10-1.29, $P<0.001$), which is statistically significant (Figure 7).

Egger's test ($P=0.113$) and Begg's test ($P=0.308$) were performed to assess possible publication bias in the reported studies (Figure 8). The absence of apparent reporting partiality was found in this study. The meta-analysis revealed minimal variability among the findings of the investigations.

Sensitivity Analysis

A robustness assessment was conducted to evaluate how individual investigations influenced the overall conclusions of the statistical synthesis (Figure 9). This analysis demonstrated that the estimated OR in the meta-

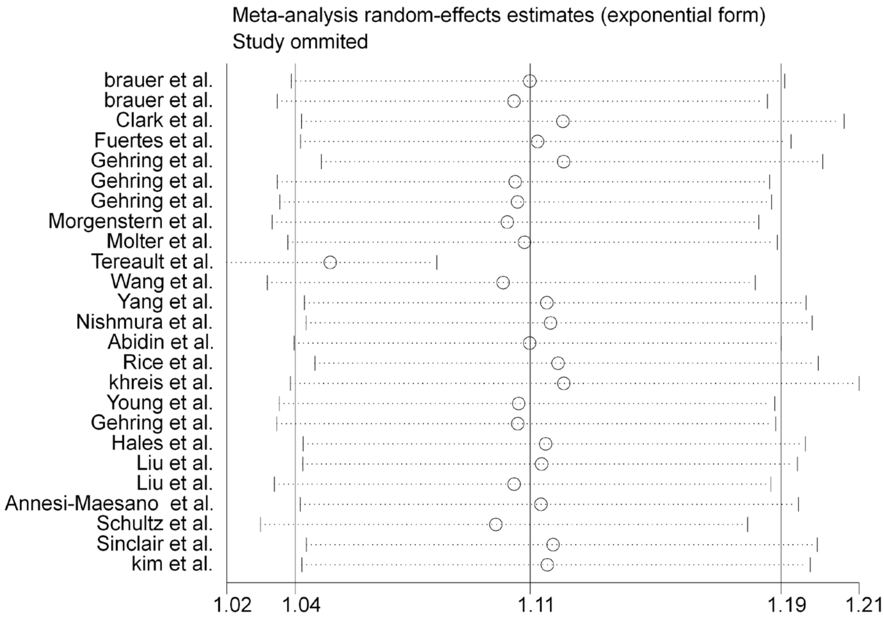

Figure 5. Sensitivity Analysis of the Association Between TRAP ($PM_{2.5}$) and the Risk of Asthma. *Note*. TRAP: Traffic-related air pollution; PM: Particulate matter

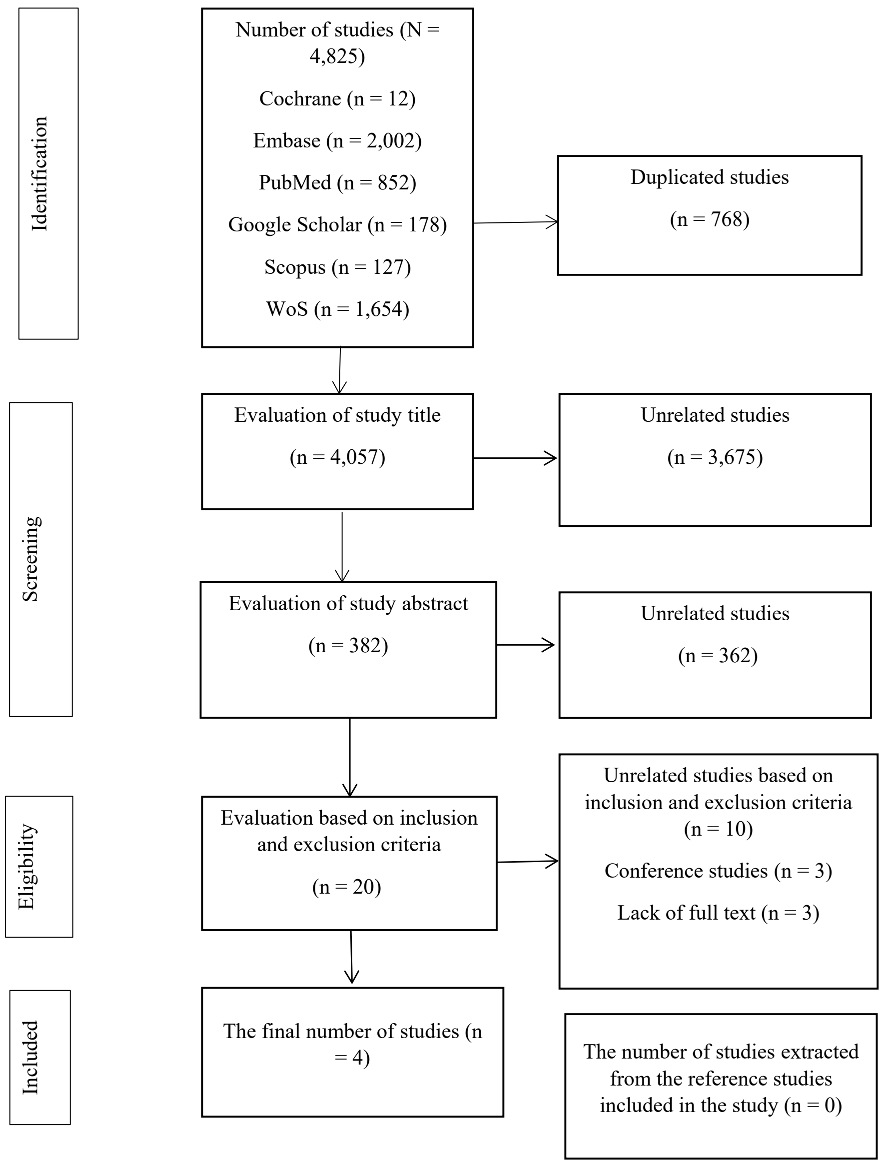

Figure 6. Flowchart of Selected Studies for Meta-analysis Assessing the Association Between Benzene and Asthma

Table 3. Features of the Studies to Explore the Connection Between TRAP (Benzene) and the Likelihood of Developing Asthma

Authors	Year	Study Design	Diagnosis Method	Study Setting	Average Age (y)	Exposure Assessment	Sample Size	OR	95% CI	Quality Score
Penard-Morand et al[52]	2010	‡	§	France	10.4	Dispersion model	9,615	1.25	1.05-1.43	9
Delfino et al[53]	2003	†	§	USA	12	Monitoring data	8,549	2.03	0.8-5.11	6
Nicolai et al[54]	2003	‡	§	Germany	10	Monitoring data	7,509	1.44	0.79-2.58	7
Hirsch et al[55]	1999	‡	§	Germany	8	Monitoring data	5,421	1.15	1.04-1.27	9

Note. OR: odds ratio; CI: Confidence interval; TRAP: Traffic-related air pollution.
†Cohort
‡Cross-sectional.
§Doctor-diagnosed.

Table 4. Adjusted Variables Modified to Investigate the Association Between TRAP (Benzene) and the Risk of Developing Asthma

Publication's First Author	Year	Adjusted Variables
Penard-morand et al[52]	2010	Age, gender, older siblings, family history of allergies, parental education level, mother's ethnicity, smoking in the household, the presence of mold or dampness, use of natural gas for heating, cooking, or water heating, and ownership of pets
Delfino et al[53]	2003	Gender, age, breastfeeding, family history of allergies, indoor environment, and new furniture in the home
Nicolai et al[54]	2003	Age, gender, hay fever or eczema, economic status, and family background of asthma
Hirsch et al[55]	1999	Age, gender, SES, smoking habits, and the like

Note. TRAP: Traffic-related air pollution; SES: Socio-Economic Status.

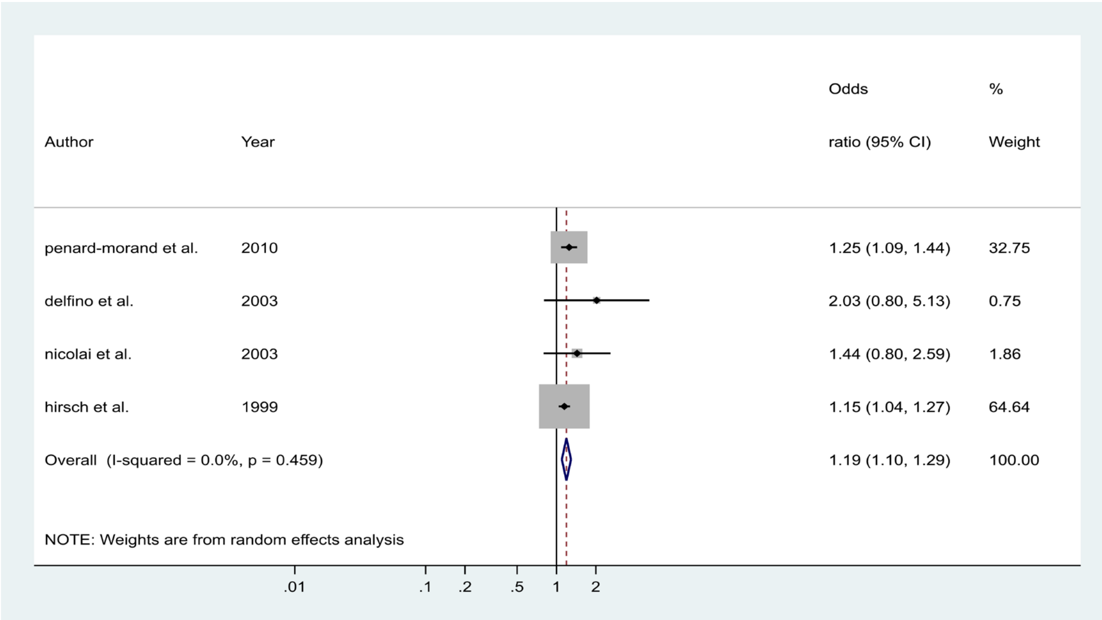

Figure 7. The Association Between TRAP (Benzene) and the Risk of Asthma. *Note*. TRAP: Traffic-related air pollution

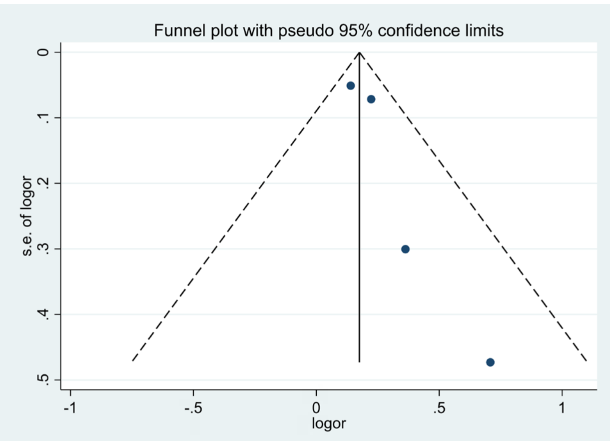

Figure 8. Assessment of Publication Bias in Meta-analyses Investigating the Association Between TRAP and Asthma Risk, Specifically Benzene. *Note*. TRAP: Traffic-related air pollution

analysis was not affected by any of the included studies, demonstrating the strength of the results.

Discussion

As there are inconsistencies regarding TRAP in the development of asthma, this systematic review and meta-analysis was conducted to evaluate the association between two important TRAP ($PM_{2.5}$ and benzene) and the occurrence of asthma.

$PM_{2.5}$

In the present study, 25 corresponding studies were examined for $PM_{2.5}$. The OR of asthma in the exposed individuals was found to be 1.11 (95% CI: 1.04-1.19, $P=0.002$), and the odds of developing asthma were statistically significant. Thus, a statistically significant

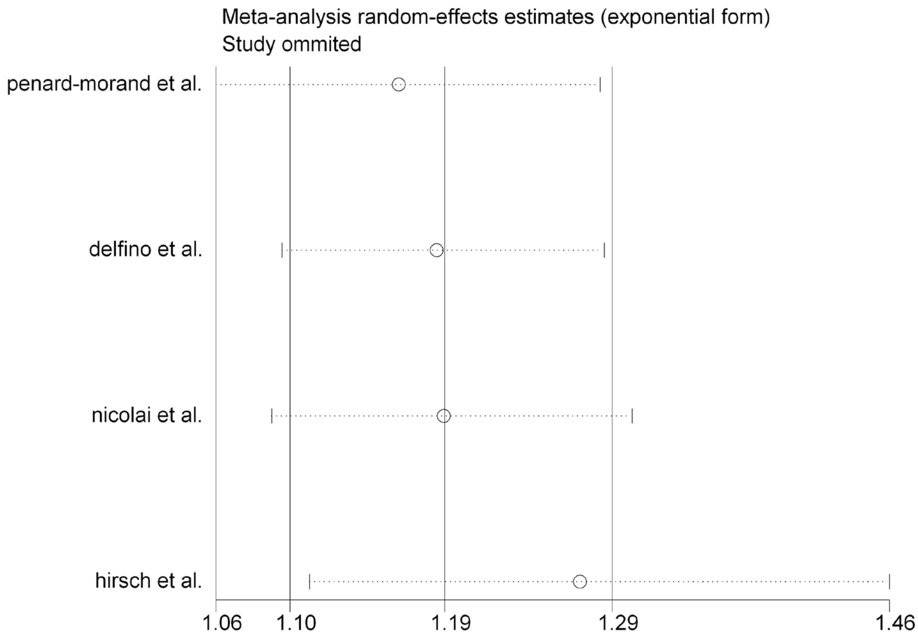

Figure 9. Sensitivity Analysis of the Association Between TRAP (Benzene) and the Risk of Asthma. *Note*. TRAP: Traffic-related air pollution

association was found between exposure to TRAP ($PM_{2.5}$) and the odds of developing asthma. $PM_{2.5}$ is a meaningful measure of air pollution, with different sources having different physicochemical compositions that can affect health differently.[56] In assessing the association between traffic-related $PM_{2.5}$ exposure and the risk of developing asthma, some studies have shown a lack of a meaningful correlation linking traffic-related $PM_{2.5}$ exposure and the risk of developing asthma. However, some studies demonstrated that this association was statistically significant, which conforms to our results. In a cohort study by Schultz et al in the United States, a notable association was observed between estimated $PM_{2.5}$ exposure and proximity to roads for asthma and allergies (OR = 1.51; 95% CI: 1.14-2.0). This population was exposed to low average annual $PM_{2.5}$ levels (about 12 µg/m^3).[57] Khreis et al reported that 15% and 33% of all annual childhood asthma cases in Bradford could be due to urban air pollution. In comparison, 7–12% of all annual childhood asthma cases could be explicitly related to TRAP.[42] In some studies, the researchers pointed out that there was a significant association between TRAP ($PM_{2.5}$) and asthma, with an OR of 1.45 (95% CI: 1.07-1.97),[37] 1.56 (95% CI: 1.03-2.37),[34] 1.31 (95% CI: 1.28-1.33),[36] and 1.19 (95% CI: 1.04-1.36).[44] In the study conducted by Brauer et al in the Netherlands, there was no significant association between TRAP ($PM_{2.5}$) and asthma, with an OR of 1.32 (95% CI: 0.96-1.83).[58] The results suggest that the odds of developing asthma and exposure to traffic-related $PM_{2.5}$ pollution are significantly higher in Asia than in regions such as the Americas, Canada, Europe, Australia, and New Zealand.

Benzene

Upon evaluating four pertinent benzene studies, it was revealed that the OR of developing asthma in individuals exposed to benzene was estimated to be 1.19 (95% CI: 1.10-1.29, $P < 0.001$), indicating a significant association between exposure to TRAP, specifically benzene, and the risk of asthma development. The majority of studies demonstrated a statistically significant association between exposure to traffic-related benzene and the potential risk of asthma onset.

In a cross-sectional study, Penard-Morand et al observed a statistically significant association between traffic-related benzene exposure and the odds of developing asthma (OR = 1.25; 95% CI: 1.08-1.43).[52] This study reinforced the robust link between lifetime asthma and benzene exposure, revealing a significant association even among children who had resided at their current address since birth. Similarly, Hirsch et al showcased a statistically significant association between asthma incidence and benzene produced from traffic (OR = 1.15; 95% CI: 1.04-1.27).[53] Contrarily, in their cohort study, Delfino et al found no significant association between TRAP (benzene) and asthma (OR = 2.03; 95% CI: 0.8-5.13).[54] Similarly, Nicoli et al reported no significant association between TRAP (benzene) and asthma (OR = 1.44; 95% CI: 0.79-2.58).[55]

This study's primary goal was to provide a comprehensive examination of the association between TRAP and the odds of developing asthma. It incorporates recent research findings and takes into account the impact of missing studies. The study conducted subgroup analyses, meta-regressions, and sensitivity analyses as part of its research methodology. These analyses aim to identify the reasons for the differences in the results of the studies included in this analysis. By conducting subgroup analyses, the study attempted to provide a more detailed account of the research findings. In general, 25 $PM_{2.5}$-related and four benzene-related studies were incorporated into our meta-analysis.

Regarding the study's limitations, some articles needed to report the desired effect size. In these cases, it was tried to calculate the relevant effect size based on other information provided in the text of the article and enter it in the final meta-analysis. The mentioned study was removed in cases where this process was impossible. The types of studies were different, and checklists and guidelines related to cohort, case-control, and cross-sectional studies were used for review.

Conclusion

According to our data, there was a positive association between TRAP exposure and the development of asthma. The results of this study confirmed that benzene and $PM_{2.5}$ could increase the odds of asthma. Future studies must investigate the association between asthma and organic pollutants in TRAP.

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Authors' Contribution

Conceptualization: Maryam Nazari, Abdollah Mohammadian-Hafshejani, Mohsen Arbabi.
Data curation: Maryam Nazari, Abdollah Mohammadian-Hafshejani, Mohsen Arbabi.
Formal analysis: Maryam Nazari, Abdollah Mohammadian-Hafshejani.
Investigation: Maryam Nazari, Abdollah Mohammadian-Hafshejani, Mohsen Arbabi.
Methodology: Maryam Nazari, Abdollah Mohammadian-Hafshejani, Mohsen Arbabi.
Project administration: Mohsen Arbabi.
Software: Abdollah Mohammadian-Hafshejani.
Supervision: Mohsen Arbabi.
Visualization: Maryam Nazari, Abdollah Mohammadian-Hafshejani, Mohsen Arbabi.
Writing–original draft: Maryam Nazari.
Writing–review & editing: Maryam Nazari, Abdollah Mohammadian-Hafshejani, Mohsen Arbabi.

Competing Interests

The authors declare that there is no conflict of interests.

Consent for Publication

Not applicable.

Data Availability Statement

All data are available in the manuscript.

Ethical Approval

The present study was approved by the Ethics Committee of Shahrekord University of Medical Sciences (with the ethical code IR.SKUMS.REC.1401.118).

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