BMC Neurology

RESEARCH

Open Access

Effect of environmental pollutants particulate matter ($PM_{2.5}$, PM_{10}), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), carbon monoxide (CO) and ground level ozone (O_3) on epilepsy

Bandar Nasser Aljafen[1], Narmeen Shaikh[2], Joud Mohammed AlKhalifah[2] and Sultan Ayoub Meo[3*]

Abstract

Background Epilepsy is a common condition that affects the brain and causes frequent seizures. Impaired brain biology is the world's fastest-growing brain disorder, and exposure to environmental pollutants is the leading cause of mental health impairment. The growing literature suggests that air pollution is an emerging cause of neurological diseases. However, the existing evidence on air pollution and epilepsy is inadequate. This study aimed to investigate the effect of environmental pollutants particulate matter ($PM_{2.5}$, PM_{10}), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), carbon monoxide (CO) and ground-level ozone (O_3) on epilepsy.

Methods This study recorded data on air pollutants and epilepsy using the electronic platforms Pub Med, Web of Science, Scopus, and Google Scholar. The keywords included for the literature search were based on two main aspects: exposure (air pollutants) and outcome (epilepsy). Initially, 78 articles and reports were identified, and after revising the abstracts and full articles, 06 studies were selected for a detailed analysis and discussion. The Odds Ratio (OR) and 95% confidence intervals (CIs) were extracted to investigate the impact between air pollutants and epilepsy. The effect of air pollution on epilepsy has been investigated through a compilation of six studies encompassing 371,515 individuals. The Cochrane chi-squared test (Chi^2), fixed-effects design was used when $I^2 < 50\%$ and $P > 0.05$; otherwise, a random-effects model was adopted.

Results The results revealed that exposure to $PM_{2.5}$ and NO_2 were positively and significantly associated with epilepsy (RR = 1.00; 95% CI: 1.00-1.01; $p = 0.03$), NO_2 (RR = 1.03; 95% CI: 1.02–1.03; $p < 0.01$). However, no association was identified between PM_{10}, SO_2, CO, and O_3 with epilepsy. The results suggest a potential association between air pollution exposure and epilepsy.

Conclusions Air pollutants $PM_{2.5}$ and NO_2 increase the risk of epilepsy. The findings suggest that reducing levels of these pollutants could be a strategic approach to mitigate neurological health risks in populations worldwide. Further research is warranted to elucidate the mechanisms and causal relationships between air pollutants and epilepsy.

*Correspondence:
Sultan Ayoub Meo
smeo@ksu.edu.sa; sultanmeo@hotmail.com

Full list of author information is available at the end of the article

Public health initiatives aimed at reducing air pollution levels and targeted interventions to protect vulnerable populations hold promise for alleviating the burden of epilepsy associated with environmental exposures.

Keywords Environmental Pollution, Particulate Matter, $PM_{2.5}$, PM_{10}, Smog Seizures, Epilepsy, Neurological Disorders

Introduction

The extensive damage caused by ambient air pollution on human health has been well-documented in the scientific literature. The initial investigations focused on respiratory, cardiovascular, and cerebrovascular systems [1–3]. However, recent studies have highlighted the deleterious impacts of air pollution on the neurological system, including impaired cognitive functions [4] and epilepsy [5].

Epilepsy is one of the most prevalent neurological diseases characterized by a predisposition to generate epileptic seizures. Epilepsy causes a sizable disease burden globally, regionally, and nationally [6, 7] and affects around 50 million people worldwide. Globally, approximately 5 million people are diagnosed with epilepsy each year, and 80% of the people with epilepsy are from low and middle-income countries [8].

Evidence suggests that air pollution induces neuroinflammation and oxidative stress in the central nervous system, contributing to the development of epilepsy [9, 10]. Particulate matter can enter the brain, triggering the release of pro-inflammatory cytokines and widespread neuroinflammation while activating astrocytes and microglia, which are detrimental to the CNS [9]. Furthermore, air pollutants, including SO_2 and NO_2, have been linked to toxic effects on nerve cell function in the CNS and cause protein oxidation, apoptosis in the hippocampus, and lipid peroxidation [11, 12].

The global literature has revealed a short-term association between air pollution and epilepsy, particularly among pollutants such as SO_2 and NO_2, indicating an elevated risk of epilepsy, especially among children [13–14]. However, the impact of air pollution on epilepsy remains incompletely understood due to inconsistent study designs, statistical approaches, and mixed findings between air pollutants and epilepsy. Therefore, this study "aimed to investigate the effect of environmental pollutants particulate matter ($PM_{2.5}$, PM_{10}), nitrogen dioxide (NO_2), carbon monoxide (CO), sulfur dioxide (SO_2) and ground-level ozone (O_3) on epilepsy".

Materials and methods

Study design and settings

This study was conducted in the "Department of Physiology, College of Medicine, King Saud University, Riyadh, Saudi Arabia," from December 1, 2023, to Jan 31, 2024.

Search strategy

The literature search was performed, and data were collected using electronic platforms such as PubMed, Embase, Google Scholar, Web of Science and Scopus to search the literature on the relationship between air pollutants and epilepsy. The keywords included a combination of two main items: exposure (air pollutants) and outcome (epilepsy). We filtered the data using the key terms "environmental pollution, air pollution, particulate matter, $PM_{2.5}$, PM_{10}, Nitrogen dioxide (NO_2), Sulfur Dioxide (SO_2), Carbon Monoxide (CO), Ozone (O_3), seizures, epilepsy". While initially using the term "environmental pollution and epilepsy," 78 documents were identified; after screening and going through the abstracts, 06 cohort studies were finally selected for a detailed analysis and discussion (Fig. 1).

Inclusion and exclusion criteria

The inclusion criteria were set as follows: Studies with exposures to air pollution ($PM_{2.5}$, PM_{10}, NO_2, SO_2, CO, O_3), and outcome was epilepsy with original research; the article language was written in English. However, the exclusion criteria include studies other than original articles, such as letters, editorials, brief communications, case reports, review articles or meta-analyses, were excluded. Moreover, studies with different outcomes that missed key information and had methodological flaws were excluded.

Statistical analysis

The statistical analyses were performed using RStudio version 4.3.2 and package 'meta.' The risk ratio (RR), % change and odds ratio (OR) with 95% confidence intervals (CIs) were extracted from the included studies. We considered the odds ratio as equivalent to relative risk, similar to the meta-analysis done in another study [15]; percentage (%) change was converted to RR using the following formula [16]: RR = 1-(%change)/100. The RR were then pooled to investigate the relationship between air pollutants and epilepsy, using the Mantel-Haenszel method [17]. For studies that reported more than one value for RR, both values were used as separate data points. Sub-group analysis was performed for studies that included the required data for male and female genders. A p-value less than $p < 0.05$ was considered significant. The "Cochrane chi-squared test (Chi^2) was used to evaluate heterogeneity among articles; a p-value < 0.05 indicates the existence of heterogeneity. To estimate the impact of heterogeneity on the analysis,

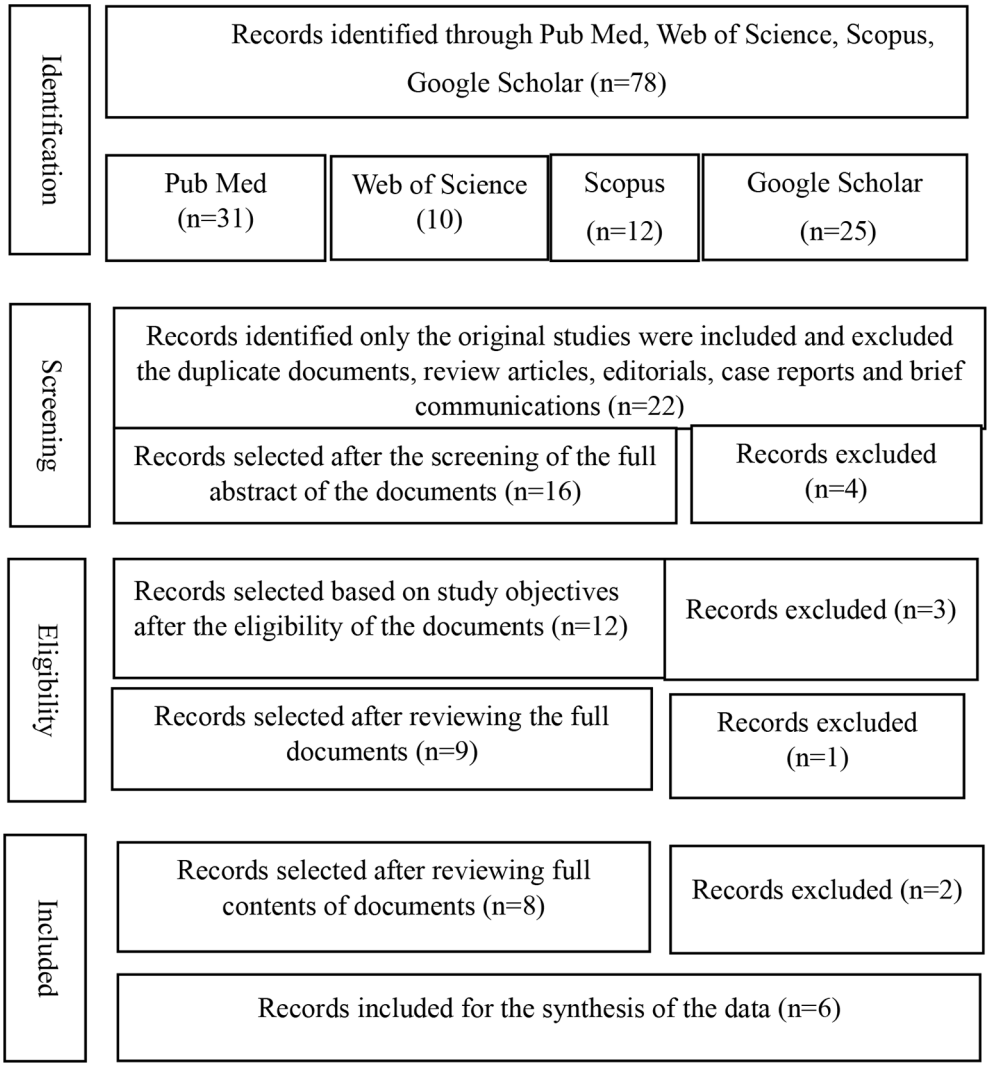

Fig. 1 PRISMA flow diagram for the selection of documents

the I^2 value was calculated. I^2 is a measure of heterogeneity and methods for calculating the associated 95% CI. I^2 expresses the proportion of variability in a meta-analysis. I^2 values ≥ 50% and $p < 0.05$ indicated a moderate to high degree of heterogeneity among pooled studies. A fixed-effects design was used when $I^2 < 50\%$ and $p > 0.05$; otherwise, a random-effects model was adopted" [18]. Egger's test was performed to evaluate publication bias, and the visual examination of the symmetry in funnel plots further assessed it. Leave-one-out sensitivity analysis was done to determine the reliability of this meta-analysis.

Risk of bias assessment

The existence of publication bias was assessed by Egger's Regression test and funnel plot. Sensitivity analysis was done to evaluate the reliability of this analysis. RStudio version 4.3.2 was used to generate both.

Sensitivity analysis

A leave-one-out sensitivity analysis was conducted to assess the overall results' robustness by determining each study's influence. The outcomes were similar when individual studies were excluded for each pollutant, which indicates that the findings were not heavily dependent on one study. The sensitivity analysis on particulate matter ($PM_{2.5}$) shows moderate sensitivity to including specific studies. Excluding some studies leads to a non-significant pooled Odds Ratio (OR) with p-values up to 0.15. However, this does not drastically change the overall effect's significance, indicating that the conclusion is not overly dependent on any single study.

Results

The impact of air pollution on epilepsy has been investigated through a compilation of six studies encompassing 371,515 individuals. Among these, approximately 60%

were male and 40% were female. These studies originate from diverse geographical locations, with three conducted in China and one in Australia, Chile, and Iran. In the subsequent sections, we present each study's outcomes and the effects observed for various pollutants. Detailed information regarding each study and its findings is outlined in Table 1.

The impact of $PM_{2.5}$ on epilepsy

In five studies focusing on the impact of $PM_{2.5}$ on epilepsy, the Cochrane chi-squared test and I2 statistic indicated insignificant heterogeneity (Chi2 = 7.81, $p = 0.17$, I2 = 36%). Therefore, a fixed model was employed. The forest plot analysis demonstrated a significant association between $PM_{2.5}$ pollutants and epilepsy (RR = 1.00; 95% CI: 1.00-1.01; $p = 0.03$) (Table 1; Fig. 2). The funnel plot suggested a small likelihood of publication bias, further confirmed by Egger's test. Additionally, leave-one-out sensitivity analysis indicated that the meta-analysis findings were robust, as excluding any single study did not alter the outcomes.

Impact of PM_{10} on epilepsy

Six studies reported the impact of PM_{10} on epilepsy. The Cochrane chi-squared test and I^2 statistic revealed a significant heterogeneity ($Chi^2 = 26.221$, $p < 0.01$, $I^2 = 77\%$), so a random effect model was used. The forest plot analysis showed that the PM_{10} pollutant was positively but not significantly associated with epilepsy (RR = 1.01; 95% CI: 0.99–1.02; $p = 0.35$) (Table 1; Fig. 3). The funnel plot indicated a slight chance of publication bias, but Egger's test showed no publication bias. Leave-one-out sensitivity analysis suggests that the meta-analysis findings were not heavily dependent on one study as the outcomes did not markedly differ when each study was excluded.

Impact of NO_2 on epilepsy

Six studies reported the impact of NO_2 on epilepsy. The Cochrane chi-squared test and I^2 statistic revealed a significant heterogeneity ($Chi^2 = 6.21$, $p = 0.40$, $I^2 = 3\%$), so a fixed effect model was used. The forest plot analysis showed that the NO_2 pollutant was positively and significantly associated with epilepsy (RR = 1.03; 95% CI: 1.02–1.03; $p < 0.01$) (Table 1; Fig. 4). The funnel plot and Egger's test showed no presence of publication bias. Leave-one-out sensitivity analysis indicates that the meta-analysis findings were not heavily dependent on one study, as the outcomes did not markedly differ when each study was excluded.

Impact of sulfur dioxide (SO_2) on epilepsy

Six studies reported the impact of SO_2 on epilepsy. The Cochrane chi-squared test and I^2 statistic revealed a significant heterogeneity ($Chi^2 = 34.07$, $p < 0.01$, $I^2 = 82\%$), so a random effect model was used. The forest plot analysis showed that the SO_2 pollutant was positively but not significantly associated with epilepsy (RR = 1.02; 95% CI: 0.99–1.05; $p = 0.23$) (Table 1; Fig. 5). The funnel plot showed some publication bias, and Egger's test showed no presence of publication bias. Leave-one-out sensitivity analysis indicates that the meta-analysis findings were not heavily dependent on one study as the outcomes did not differ markedly when each study was excluded.

Impact of carbon monoxide (CO) on epilepsy

Five studies reported the impact of CO on epilepsy. The Cochrane chi-squared test and I^2 statistic revealed a significant heterogeneity ($Chi^2 = 23.83$, $p < 0.01$, $I^2 = 83\%$), so a random effect model was used. The forest plot analysis showed that the CO pollutant was positively but not significantly associated with epilepsy (RR = 1.02; 95% CI: 0.96–1.09; $p = 0.38$) (Table 1; Fig. 6). The funnel plot showed some publication bias, and Egger's test showed no publication bias. Leave-one-out sensitivity analysis indicates that the meta-analysis findings were not heavily dependent on one study, as the outcomes did not markedly differ when each study was excluded.

Impact of ground-level ozone (O_3) on epilepsy

Five studies reported the impact of O_3 on epilepsy. The Cochrane chi-squared test and I^2 statistic revealed a significant heterogeneity ($Chi^2 = 27.76$, $p < 0.01$, $I^2 = 82\%$), so a random effect model was used. The forest plot analysis showed that the O_3 pollutant was not significantly associated with epilepsy (RR = 1.00; 95% CI: 0.97–1.03; $p < 0.01$) (Table 1; Fig. 7). The funnel plot showed some publication bias, and Egger's test showed no publication bias. Leave-one-out sensitivity analysis indicates that the meta-analysis findings were not heavily dependent on one study, as the outcomes did not markedly differ when each study was excluded.

Discussion

The present study investigates the impact of environmental pollutants $PM_{2.5}$, PM_{10}, NO_2, SO_2, CO, and ground-level ozone (O_3) on epilepsy. We found a significant link between air pollutants $PM_{2.5}$ and NO_2 and epilepsy. These pollutants, commonly found in urban areas due to vehicle emissions and industrial activities, are potent stressors affecting the central nervous system. This study's findings emphasize the importance of considering environmental factors in understanding the pathophysiology of epilepsy. This insight leads to discussions about how these pollutants affect the brain, potential public health interventions, and the need for further research. It is crucial to place these findings in the context of existing knowledge and explore the direct and indirect pathways through which $PM_{2.5}$ and NO_2 impact epileptic seizures.

Table 1 Air pollutants and their effect on epilepsy

Author, Year, Country	Study design	Sample Size	Overall Epilepsy Outcome	
Farahmandfard et al. 2022, Iran [19]	Ecological Study	Total cases: 894 Men: 498 Women: 396	$PM_{2.5}$	RR (95% CI): 1.0017 (0.9977–1.0057). For a mean concentration of 27.46 µg/m3, no significant association with hospital admissions
			PM_{10}	RR (95% CI): 1.0037 (1.0024–1.0050) For a mean concentration of 71.11 µg/m3, a positive significant association with hospital admissions
			NO_2	RR (95% CI): 1.0266 (1.0168–1.0364). A positive, significant association with admissions was found for a mean concentration of 15.82 ppb.
			O_3	RR (95% CI): 0.9816 (0.9756–0.9877). For a mean concentration of 30.21ppb, there was no association with hospital admissions.
			CO	RR (95% CI): 0.9008 (0.7906–1.0263). For a mean concentration of 1.07ppm, there was no significant association with hospital admissions.
			SO_2	RR (95% CI): 0.9978 (0.9945–1.0011). For a mean concentration of 26.12 ppm, there is no significant association with admissions.
Chen Z et al. 2022, Australia [20]	Time-stratified case-crossover	Total cases: 49 Males: 22 Females: 27	PM_{10}	RR (95% CI): 1.00 (0.97, 1.03). For a median concentration of 15 µg/m3, there was no association with epileptic seizures.
			NO_2	RR (95% CI): 1.04 (0.98, 1.10). For a median concentration of 6.78ppb, there is a positive but not significant association with epileptic seizures.
			O_3	RR (95% CI): 0.99 (0.94, 1.05). For a median concentration of 14.74 ppb, there was no association with epileptic seizure.
			CO	RR (95% CI): 1.04 (1.01, 1.07). For a median concentration of 0.15ppm, there was a positive significant association with epileptic seizures.
			SO_2	RR (95% CI): 0.98 (0.95, 1.00). For a median concentration of 0.30ppb, there is no association with epileptic seizures.
Xu C et al., 2016, China [21]	Time series	Total cases: 20,368 Males: 12,041 Females: 8327	$PM_{2.5}$	95% CI: 0.20 (-0.23, 0.62). A 10 µg/m3 increase was associated with positive but insignificant outpatient visits of epilepsy patients.
			PM_{10}	95% CI: 0.14 (-0.13, 0.41. A 10 µg/m3 increase was associated with positive but insignificant outpatient visits of epilepsy patients.
			NO_2	95% CI: 3.17 (1.41, 4.93). 10 µg/m3 increase was associated with significantly positive outpatient visits of epilepsy patients.
			O_3	95% CI: -0.84 (-1.58, -0.09). 10 µg/m3 increase was associated with significantly decreased outpatient visits of epilepsy patients.
			CO	95% CI: 0.11 (-0.37, 0.59). A 0.1 mg/m3 increase was associated with positive but not significant outpatient visits.
			SO_2	95% CI: 3.55 (1.93, 5.18). A 10 µg/m3 increase was associated with significantly positive outpatient visits.
Bao X et al. 2019, China [22]	Time-stratified case-crossover	Total cases: 51,523 Men: 30,908 Women: 20,615	$PM_{2.5}$	95% CI: 0.6 (-0.7,1.9). The increase in IQR (56.9 µg/m3) was positively but not significantly associated with hospitalization.
			PM_{10}	95% CI: 0.1 (-1.3,1.5). IQR (77.5 µg/m3) increase was positively but not significantly associated with hospitalization
			NO_2	95% CI: 2.0 (0.5,3.6). An IQR (25.9 µg/m3) increase was positively and significantly associated with hospitalization.
			CO	95% CI): 1.1 (0.1,2.1). An IQR (0.5 µg/m3) increase was positively and significantly associated with hospitalization.
			SO_2	95% CI: 0.8 (-0.5,2.1). An IQR (18.9 µg/m3) increase was positively but not significantly associated with hospitalization.
Cakmak S et al. 2010, Chile [23]	Time series	Total cases: 290,500	$PM_{2.5}$	RR (95% CI): 1.065 (1.002, 1.132). An IQR (32.48 µg/m3) increase in $PM_{2.5}$ was associated with increased hospitalizations.
			PM_{10}	RR (95% CI): 1.083 (1.038, 1.13). An IQR (72.24 µg/m3) increase in PM_{10} was associated with increased hospitalizations.
			NO_2	RR (95% CI): 1.108 (1.021, 1.204). An IQR (44.74ppb) increase in NO_2 was associated with increased hospitalizations.
			O_3	RR (95% CI): 1.100 (1.025, 1.181). An IQR (93.26ppb) increase in O_3 was associated with increased hospitalizations.
			CO	RR (95% CI): 1.098 (1.045, 1.155). An IQR (1.11ppm) increase in CO was associated with increased hospitalizations.
			SO_2	RR (95% CI): 1.085 (1.03, 1.144). An IQR (9.32ppb) increase in SO_2 was associated with increased hospitalizations.

Table 1 (continued)

Author, Year, Country	Study design	Sample Size	Overall Epilepsy Outcome	
Cheng J et al. 2022, China [24]	Time-stratified case-crossover	Total cases: 8181 Age: 0–18 years Boys: 4860 Girls: 3321	$PM_{2.5}$	OR (95% CI); A: Warm season: 1.001 (0.979, 1.022); B: Cold season: 1.014 (1.002, 1.025). 10 µg/m3 increase was not significantly associated with increased hospitalization for either season
			PM_{10}	OR (95% CI); A: Warm season: 0.996 (0.985, 1.008); B: Cold season: 1.014 (1.005, 1.022). 10 µg/m3 increase was not associated with increased hospitalization for the warm season but was a significant positive increase for the cold season.
			NO_2	OR (95% CI); A: Warm season: 1.004 (0.968, 1.041); B: Cold season: 1.035 (1.011, 1.059). 10 µg/m3 increase was not significantly associated with increased hospitalization for either season
			O_3	OR (95% CI); A: Warm season: 1.011 (0.997, 1.025); B: Cold season: 1.004 (0.981, 1.027). 10 µg/m3 increase was not significantly associated with increased hospitalization for either season
			SO_2	OR (95% CI); A: Warm season: 1.006 (0.889, 1.138); B: Cold season: 1.046 (0.965, 1.134). 10 µg/m3 increase was not significantly associated with increased hospitalization for either season

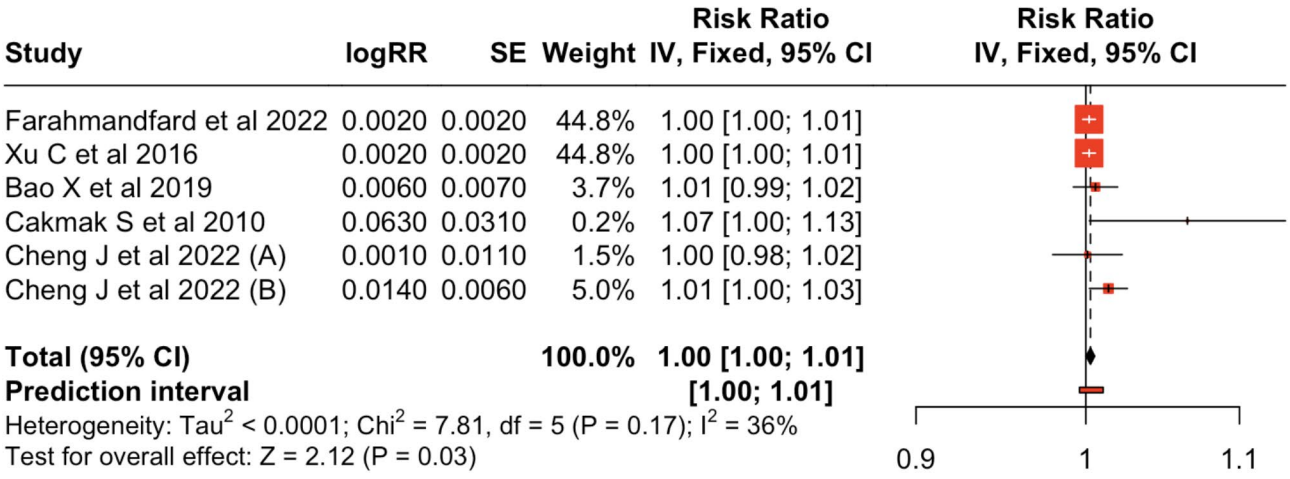

Fig. 2 Impact of $PM_{2.5}$ on Epilepsy. *(**A**) and (**B**) are two RRs from within the same study and are used as separate data points

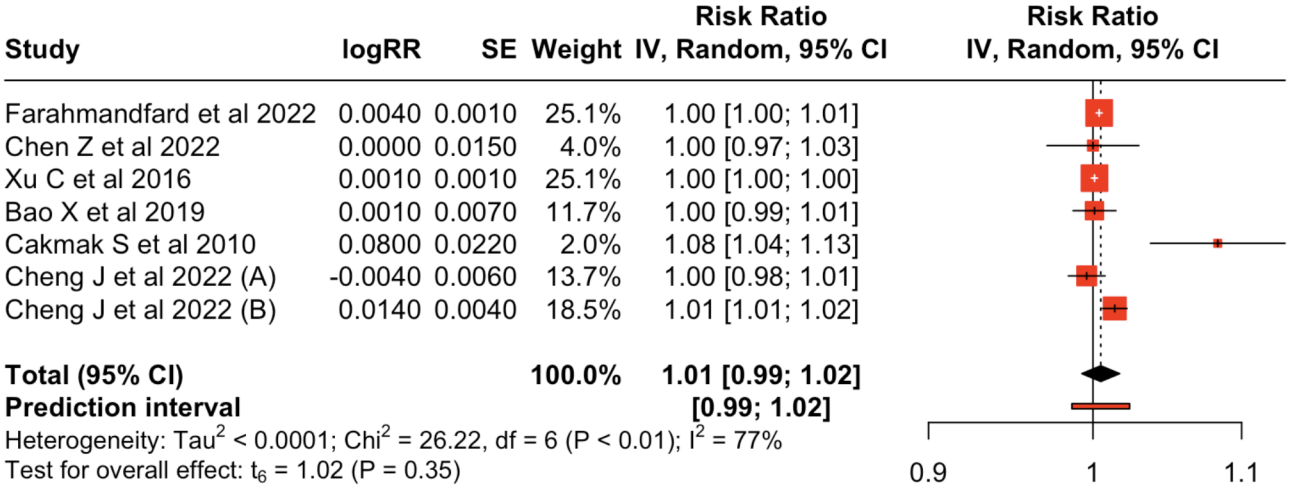

Fig. 3 Impact of PM_{10} on Epilepsy. *(**A**) and (**B**) are two RRs from within the same study and are used as separate data points

The relationship between air pollution and neurological health, especially epilepsy, is a growing concern in environmental health. This discussion summarizes evidence from recent studies on the impact of specific air pollutants $PM_{2.5}$, PM_{10}, NO_2, CO, SO_2, and ground-level O_3 on epilepsy incidence and seizure frequency.

The literature shows a significant link between $PM_{2.5}$ and PM_{10} exposure and increased seizure risk in individuals with epilepsy. The delicate and coarse particulate

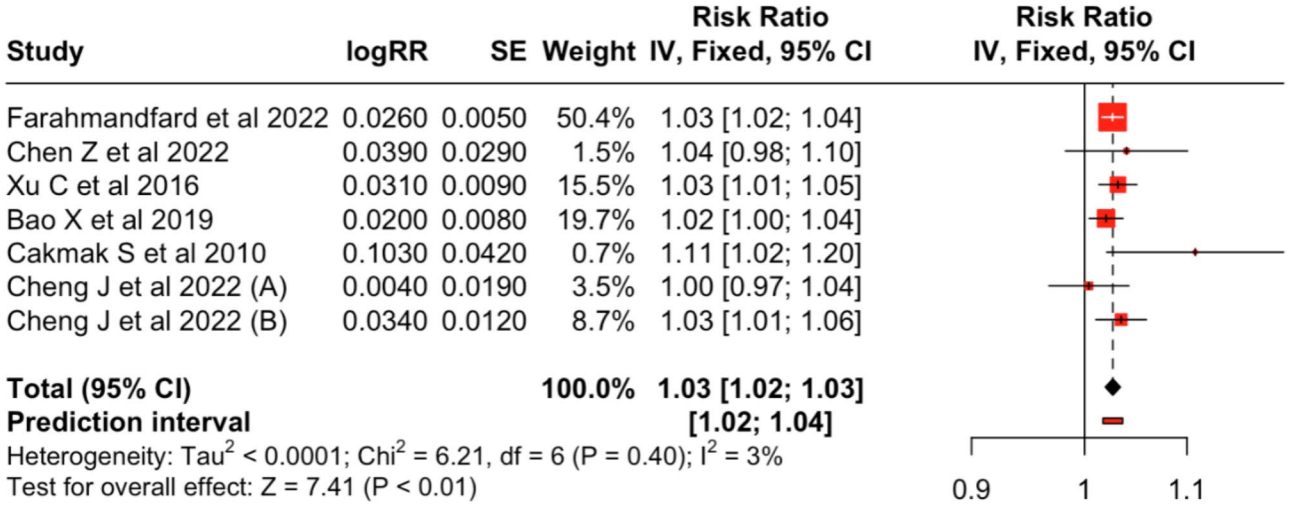

Fig. 4 Impact of NO_2 on Epilepsy. *(**A**) and (**B**) are two RR from within the same study and are used as separate data points

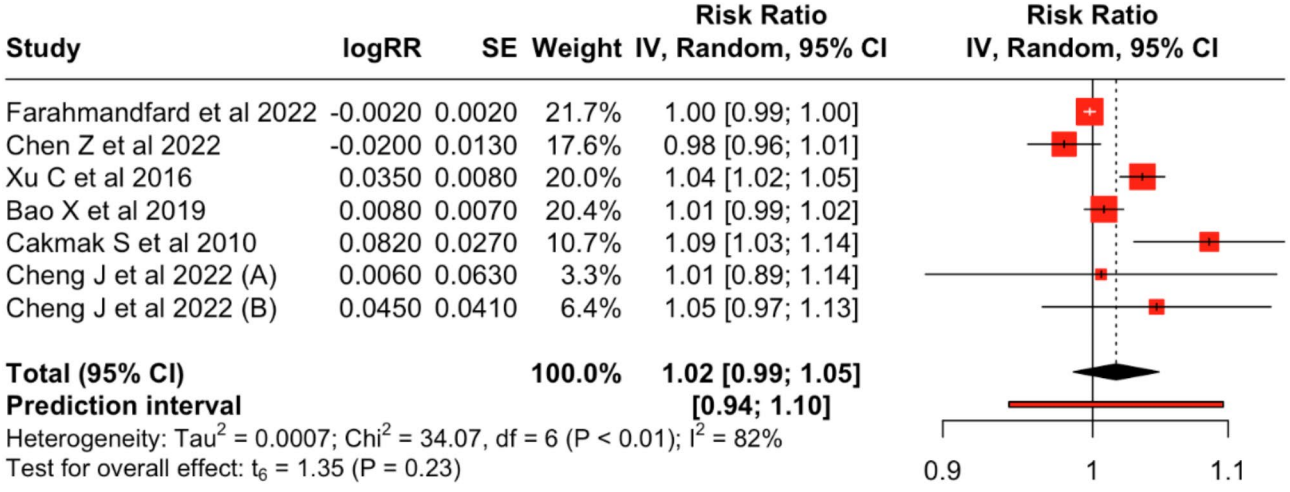

Fig. 5 Impact of SO_2 on Epilepsy

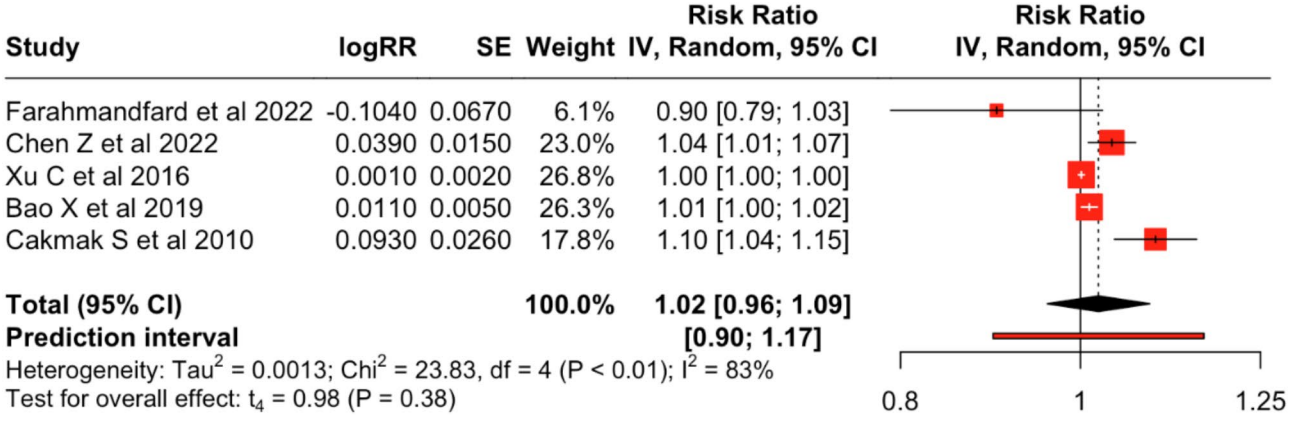

Fig. 6 Impact of CO on Epilepsy

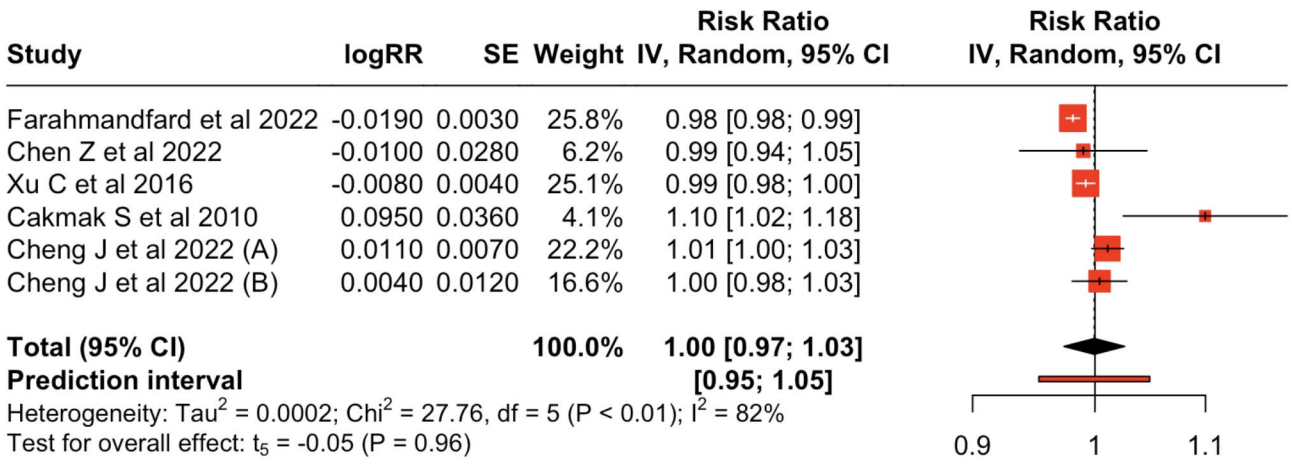

Fig. 7 Impact of Ground Level O_3 on Epilepsy. * (**A**) and (**B**) are two RR from within the same study and are used as separate data points

matter may worsen respiratory conditions, leading to hypoxemia, a known seizure trigger. Additionally, the inflammatory response induced by particulate matter may contribute to neuronal excitability, facilitating seizures [25].

The NO_2 exposure has been associated with a higher risk of epilepsy development, disrupting the blood-brain barrier and leading to neuroinflammation and increased seizure susceptibility, especially in urban areas with high vehicular emissions [26]. Although less researched about epilepsy, CO exposure has been linked to neurological damage that may predispose individuals to seizures. Acute CO poisoning can cause hypoxic injury, potentially triggering seizures in susceptible individuals [27].

The emerging evidence suggests that SO_2 exposure may have neurotoxic effects that alter central nervous system functioning [28]. However, the exact pathways through which SO_2 exposure might influence seizure activity remain fully elucidated. Inhalation of O3, a potent oxidant, causes oxidative stress and inflammation within the respiratory system, which could indirectly affect neurological health. While direct evidence linking O_3 exposure to epilepsy is limited, the potential for O_3 to exacerbate underlying conditions that trigger seizures warrants further investigation [29].

In our comprehensive analysis of the environmental factors influencing epilepsy, focusing on air pollutants like $PM_{2.5}$ and NO_2, we identified a correlation with epilepsy incidence. However, diverse viewpoints in the literature, such as the Xu et al. study [21], demonstrated a complex relationship between air pollution and epilepsy and suggested nuanced findings. For example, a 10 μg/m^3 increase of NO_2 and SO_2 was linked to a 3.17% and 3.55% rise in outpatient visits for epilepsy. The NO_2 and SO_2 were positively related to outpatient visits for epilepsy. This indicates that the impact of air pollutants on epilepsy may vary based on the type of pollutant and other environmental or genetic factors.

Yang et al. [30] reported that $PM_{2.5}$, PM_{10}, and SO_2 are common air pollutants that affect the occurrence of convulsions in children. $PM_{2.5}$ and SO_2 are risk factors; an increase in the level of $PM_{2.5}$ could increase the occurrence of child convulsions. The highest incidence of convulsions was observed in children 1 to 2 years old, and it was higher in boys than in girls. Similarly, the present study identified $PM_{2.5}$ and NO_2 as central air pollutants that increase the risk of epilepsy.

Another study in Kerman, Iran, by Farahmandfard et al. (2022) [19] suggested that certain air pollutants could be risk factors for epilepsy and hospital admission, reinforcing the connection between air quality and neurological health. However, the roles of different pollutants and their mechanisms of action remain complex and not fully understood, as highlighted by Kawakami et al. [31] study on nitric oxide fractions in the epilepsy-prone mouse brain, which explored potential biochemical pathways in epileptogenesis.

The present study findings are significant in relation to the epidemiological data from the World Health Organization (WHO) to illustrate how even a small percentage (1%) increase in risk rate can have substantial implications for the global epidemiology of epilepsy. The epidemiological data from the WHO [8] demonstrates that 50 million people worldwide have epilepsy, and approximately 5 million new cases are diagnosed with epilepsy each year [8]. A 1% increase in risk, though statistically reasonable, would correspond to an estimated 500,000 additional cases globally and 50,000 new cases per annum. This 1% increase could exacerbate health inequities and strain already overburdened healthcare systems. The present study findings provide a better understanding of the impact of air pollution on epilepsy and public health significance, strengthening the epidemiological

and clinical implications of the study findings. The findings emphasize the complexity of the relationship between air pollution and epilepsy, underscoring the need for further research to unravel air pollutants' direct and indirect effects on neurological health. The divergent results and methodologies of these studies highlight the importance of a multifaceted approach to understanding the environmental determinants of epilepsy and informing public health interventions and policy.

Pathophysiological mechanisms

The exact mechanisms by which air pollution contributes to epilepsy are still being investigated. Several plausible pathways have been proposed, including neuroinflammation, oxidative stress, alteration of neurotransmitter systems, and neuronal damage. These pathophysiological conditions damage the cellular structures and disrupt normal neuronal function, potentially contributing to the development of epilepsy [32, 33]. At the same time, further research is needed to fully elucidate the relationship between air pollution and epilepsy. Air pollution continues to rise globally, and efforts to reduce emissions and mitigate the impact of pollution on human health are more critical than ever. Additionally, healthcare providers should be aware of the potential link between pollution and epilepsy when evaluating and managing patients with this condition. Addressing pollution at both individual and societal levels is essential to create a healthier environment and reduce the burden of neurological disorders such as epilepsy.

Study strengths and limitations

Similar to other studies, this study has some strengths and limitations. This study investigated and highlighted a critical topic: the impact of air pollutants on epilepsy. This is the first study to highlight the effects of air pollutants on epilepsy and provide a comprehensive understanding of the pathophysiological phenomenon, enhancing generalizability across different settings and conditions. We identified the publication bias by including a more balanced and unbiased estimate of the actual effect size. The limitations of this study include the limited availability of literature; hence, our analysis is based on the six studies. Despite the efforts to include published studies from leading science journals, publication bias remains a concern in analysis. Overall, in this study, we synthesized the evidence and interpreted the findings in the appropriate context.

Conclusion

The study findings emphasize the impact of air pollutants on epilepsy, highlighting the intricate mechanisms through which environmental factors contribute to the pathophysiology of seizures. These findings underscore the need for enhanced public health initiatives to reduce air pollution levels and further research to elucidate the complex interactions between air quality and neurological disorders. Addressing air pollution not only improves overall health but also offers a potential pathway to mitigate the burden of epilepsy, thereby improving the quality of life for those affected by this condition.

Abbreviations

PM	Particulate matter
NO_2	Nitrogen dioxide
SO_2	Sulfur dioxide
CO	Carbon monoxide
O_3	Ozone

Acknowledgements

We thank the researchers supporting project number RSP 2025 R47, King Saud University, Riyadh, Saudi Arabia.

Author contributions

BNJ, NS, JAK: literature review, data collection and analysis, and review of the manuscript. SAM: conceptualization, literature review, writing and editing; all authors have read and approved to publish the manuscript.

Funding

King Saud University, Riyadh, Saudi Arabia (RSP 2025 R47).

Data availability

The raw data supporting the conclusions of this article may be provided on reasonable request to the corresponding author.

Declarations

Ethics statement and consent to participate

This study was exempted from ethical approval and consent because data was obtained from publicly available literature.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Medicine (Neurology Unit), College of Medicine, King Saud University, Riyadh 11461, Saudi Arabia
[2]College of Medicine, King Saud University, Riyadh 11461, Saudi Arabia
[3]Department of Physiology, College of Medicine, King Saud University, Riyadh 11461, Saudi Arabia

Received: 16 March 2024 / Accepted: 19 March 2025
Published online: 01 April 2025

References

1. Cohen AJ, Brauer M, Burnett R. Estimates and 25-year trends of the global disease burden attributable to ambient air pollution: an analysis of data from the global burden of diseases study 2015. Lancet. 2017;389(10082):1907–18.
2. Newell K, Kartsonaki C, Lam KBH, Kurmi OP. Cardiorespiratory health effects of particulate ambient air pollution exposure in low-income and middle-income countries: a systematic review and meta-analysis. Lancet Planet Health. 2017;1(9):e368e80.
3. Verhoeven JI, Allach Y, Vaartjes ICH, Klijn CJM, de Leeuw FE. Ambient air pollution and the risk of ischaemic and haemorrhagic stroke. Lancet Planet Health. 2021;5(8):e542e52.
4. Meo SA, Salih MA, Al-Hussain F, Alkhalifah JM, Meo AS, Akram A. Environmental pollutants $PM_{2.5}$, PM_{10}, carbon monoxide (CO), nitrogen dioxide (NO_2),

sulfur dioxide (SO_2), and Ozone (O_3) impair human cognitive functions. Eur Rev Med Pharmacol Sci. 2024;28(2):789–96. https://doi.org/10.26355/eurrev_202401_35079.
5. Mei H, Wu D, Yong Z, Cao Y, Chang Y, Liang J, Jiang X, Xu H, Yang J, Shi X, Xie R, Zhao W, Wu Y, Liu Y. PM2.5 exposure exacerbates seizure symptoms and cognitive dysfunction by disrupting iron metabolism and the Nrf2-mediated ferroptosis pathway. Sci Total Environ. 2024;910:168578. https://doi.org/10.1016/j.scitotenv.2023.168578.
6. Guerrini R. Epilepsy in children. Lancet. 2006;367(9509):499–524.
7. GBD 2016 Epilepsy Collaborators. Global, regional, and National burden of epilepsy, 1990–2016: a systematic analysis for the global burden of disease study 2016. Lancet Neurol. 2019;18(4):357–75.
8. World Health Organization (WHO). Epilepsy. Available at: https://www.who.int/news-room/fact-sheets/detail/epilepsy. Cited date Feb 2, 2024.
9. Fernandes MJS, Carletti CO, Sierra de Araújo LF, Santos RC, Reis J. Respiratory gases, air pollution and epilepsy. Rev Neurol (Paris). 2019;175(10):604–13.
10. Hahad O, Lelieveld J, Birklein F, Lieb K, Daiber A, Münzel T. Ambient air pollution increases the risk of cerebral and neuropsychiatric disorders through the induction of inflammation and oxidative stress. Int J Mol Sci. 2020;21(12):4306.
11. Farahani H, Hasan M. 1992. Nitrogen dioxide induced changes in the level of free fatty acids, triglyceride, esterified fatty acid, ganglioside, and lipase activity in the guinea pig brain. J Environ Sci Health B. 1992; 27 (1): 53–71.
12. Sang N, Hou L, Yun Y, Li G. SO_2 inhalation induces protein oxidation, DNA-protein crosslinks, and apoptosis in rat hippocampus. Ecotoxicol Environ Saf. 2009;72(3):879–84.
13. Yalçın G, Sayınbatur B, Toktaş İ, Gürbay A. The relationship between environmental air pollution, meteorological factors, and emergency service admissions for epileptic attacks in children. Epilepsy Res. 2022;187:107026. https://doi.org/10.1016/j.eplepsyres.2022.107026. Epub 2022 Sep 30. PMID: 36252382.
14. Chiang KL, Lee JY, Chang YM, Kuo FC, Huang CY. The effect of weather, air pollution and seasonality on the number of patient visits for epileptic seizures: A population-based time-series study. Epilepsy Behav. 2021;115:107487. https://doi.org/10.1016/j.yebeh.2020.107487.
15. Lee KK, Spath N, Miller MR, Mills NL, Shah ASV. Short-term exposure to carbon monoxide and myocardial infarction: A systematic review and meta-analysis. Environ Int. 2020;143:105901. https://doi.org/10.1016/j.envint.2020.105901.
16. Julian PTH, Li T, Jonathan JD, Julian PT, Higgins J, Thomas J, Chandler M, Cumpston T, Li MJ, Page. Vivian Welch. 2019. https://doi.org/10.1002/9781119536604.ch6.
17. Fidler V, Nagelkerke N. The Mantel-Haenszel procedure revisited: models and generalizations. Speybroeck N, éditeur. PLoS ONE. 2013;8:e58327.
18. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. A basic introduction to fixed-effect and random-effects models for meta-analysis. Res Synth Method. 2010;1:97–111.
19. Farahmandfard MA, Ebrahimi HA, Khanjani N, Mirzaee M. Air pollution and hospital admission for epilepsy in Kerman, Iran. Health Scope. 2022;11(3):e124245. https://doi.org/10.5812/jhealthscope-124245.
20. Chen Z, Yu W, Xu R, Karoly PJ, Maturana MI, Payne DE, Li L, Nurse ES, Freestone DR, Li S, Burkitt AN, Cook MJ, Guo Y, Grayden DB. Ambient air pollution and epileptic seizures: A panel study in Australia. Epilepsia. 2022;63(7):1682–92. https://doi.org/10.1111/epi.17253.
21. Xu C, Fan Y-N, Kan H-D, Chen R-J, Liu JH, Li Y-F, et al. The novel relationship between urban air pollution and epilepsy: A time series study. PLoS ONE. 2016;11(8):e0161992. https://doi.org/10.1371/journal.pone.0161992.
22. Bao X, Tian X, Yang C, Li Y, Hu Y. Association between ambient air pollution and hospital admission for epilepsy in Eastern China. Epilepsy Res. 2019;152:52–8. https://doi.org/10.1016/j.eplepsyres.2019.02.012.
23. Cakmak S, Dales RE, Vidal CB. Air pollution and hospitalization for epilepsy in Chile. Environ Int. 2010;36(6):501–5. https://doi.org/10.1016/j.envint.2010.03.008.
24. Cheng J, Su H, Song J, Wang X. Short-term effect of air pollution on childhood epilepsy in Eastern China: A space-time-stratified case-crossover and pooled analysis. Environ Int. 2022;170:107591. https://doi.org/10.1016/j.envint.2022.107591.
25. Johnson K, Lee A. Inflammatory responses to PM2.5 and seizure susceptibility. J Neuroinflamm. 2020;17(1):45.
26. Green R, et al. Nitrogen dioxide exposure and neuroinflammatory markers in epilepsy patients. Environ Res Lett. 2021;16(4):044042.
27. Brown T, Harris G. Carbon monoxide exposure and neurological outcomes: A review. Toxicol Rep. 2022;9:1049–56.
28. Miller S, White R. Sulfur dioxide exposure and its potential neurotoxic effects: emerging evidence. J Toxicol Sci. 2023;48(1):13–21.
29. Wilson K, et al. Ozone exposure and oxidative stress: implications for the pathogenesis of neurological diseases. Environmental Health Perspectives; 2021.
30. Yang L, Sun L, Chu W, Zhu Y, Wu G. Study of the impact of air pollution on convulsions in children: A Hospital-Based retrospective study in Hangzhou, China. Clin Pediatr (Phila). 2023;62(10):1186–92. https://doi.org/10.1177/00099228231154059.
31. Kawakami Y, Murashima YL, Tsukimoto M, Okada H, Miyatake C, Takagi A, Ogawa J, Itoh Y. The roles of dominance of the nitric oxide fractions nitrate and nitrite in the Epilepsy-Prone EL mouse brain. JNMS. 2021;88(3). https://doi.org/10.1272/jnms.JNMS.2021_88-402.
32. Patel M. Mitochondrial dysfunction and oxidative stress: cause and consequence of epileptic seizures. Free Radic Biol Med. 2004;37(12):1951–62.
33. Vezzani A, Granata T. Brain inflammation in epilepsy: experimental and clinical evidence. Epilepsia. 2005;46(11):1724-43. https://doi.org/10.1111/j.1528-1167.2005.00298.x.

Publisher's note