

Air Pollution and Headache Disorders

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Abstract

Air pollution, the most prevalent form of pollution worldwide, is associated with a wide range of neurological disorders, including neurodegenerative conditions, stroke, autism, depression, and developmental delay. There is accumulating evidence on the association between air pollution and headache disorders, especially migraine. Many classical and non-classical air pollutants have been associated with headache, including particulate matter, nitrogen dioxide, sulfur dioxide, ozone, carbon monoxide, as well as polycyclic aromatic hydrocarbons and volatile organic compounds. There has also been research on the impact of biomass fuels on health-related symptoms, including headache, which form an important source of air pollution in our country. The exact mechanisms underlying headache pathophysiology vis-à-vis air pollution are not precisely defined but include triggering of neuroinflammation and activation of the transient receptor potential ankyrin 1 (TRPA1)-associated pathways. Evidence from different regions of the world indicates a significant association between headache incidence and prevalence, and occurrence of air pollution. Despite growing data, research on adverse effects of air pollution on headache disorders remains limited, and appropriate outcome measures are not holistically defined in these studies. Due to the rapid advancement of the scourge of air pollution, there is a pressing need to expand the arena of research, specifically focused on pathological mechanisms, impact on health and quality-of-life parameters, as well as broader global ramifications.

Keywords: Migraine, nitrogen dioxide, particulate matter, pollution, sulfur dioxide

INTRODUCTION

Headache ranks as a leading cause of disability worldwide, as per The Global Burden of Disease study, contributing the third highest years lived with disability (YLD), following low back pain and depression.^[1] The most frequent headache disorders globally comprise migraine, tension-type headache, and medication-overuse headache. Migraine itself contributes as the second most common cause of disability in the world, and the highest among females.^[2] Moreover, there has been increasing recognition of the psychosocial, economic, and vocational burden of headache disorders. Considering the high extent of disability associated with headache disorders, it is crucial to recognize and ameliorate all potentially preventable risk factors. The impact of environmental factors on migraine and headache disorders in general has been the subject of much discussion in the literature.^[3]

Air pollution is the most prevalent form of pollution and is known to adversely affect respiratory, neurobehavioral, cardiovascular, and immunological systems.^[4] It accounts for seven million deaths annually. Consequently, recognizing its perilous impact, the latest World Health Organization (WHO) air quality guidelines have further reduced the level of air pollutants considered to be acceptable.^[5]

Air pollution exerts its hazardous effects via many harmful subcomponents. These include classical pollutants such as particulate matter (PM), which comprises particles of very small size. These are inspired into the respiratory system, extend harmful effects on the respiratory, cardiovascular, nervous, and reproductive systems, and contribute toward

malignancies. PM_{2.5} comprises fine PM, with particles <2.5 micrometer in aerodynamic diameter. The classical pollutants include nitrogen dioxide (NO₂), carbon monoxide (CO), sulfur dioxide (SO₂), and ozone (O₃). Other pollutants include dioxins, polycyclic aromatic hydrocarbons (PAH), volatile organic compounds, and several more. While outdoor air pollution refers to ambient air pollution, indoor pollution refers to pollution generated due to the combustion of household fuels. Common sources of outdoor air pollution include industrial and agricultural processes and fossil fuel combustion.

Multiple neurological disorders, including neurodegenerative conditions such as Alzheimer disease and Parkinson disease, stroke, autism, dementia, low birth weight, and psychological issues such as depression, have been linked to long-term exposure to air pollutants.^[6-11] There are also links between

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multiple sclerosis prevalence and relapse and ambient air pollution.^[12]

In recent literature, ambient air pollution has been increasingly reported as a risk factor for migraine. Patients with migraine report subjective exacerbation of symptoms with worsening of air quality. High air pollution levels have been associated with increased emergency visits to hospitals. Higher levels of particulate matter had been associated with exacerbations of migraine. The mechanisms linking headache and air pollution may be engendered in abnormalities in neurotransmitter systems, neuroinflammation, and subsequent neuronal damage.

In view of accruing evidence in the literature on the interlinkage between headache disorders and air pollution, a comprehensive review is the need of the hour. In this narrative review, we aimed to describe the association, pathogenesis, and treatment concerns pertinent to headache in relation to air pollution.

Search methodology

We performed a search using PubMed and Google Scholar databases on December 2, 2021, using the following search terms: “Air pollution” AND “headache.” We included clinical trials, observational studies, case–control studies, systematic reviews, and meta-analyses. We included studies in the English language only. We also included relevant cross-references. We excluded narrative reviews, lone abstracts, letters, case series, and case reports. After screening and excluding duplicates, titles and abstracts of 108 studies that remained were screened. Full texts of these 89 studies were accessed, and ultimately, 54 studies were included in this review.

Pathophysiology linking headache and air pollution

The interlinking pathophysiology between headache and air pollution may be best understood in the context of adverse effects of air pollution on brain health, in general. Air pollutants gain access to the nervous system either through the olfactory tract, via the lower respiratory tract, or through the systemic circulation.^[13] Some of these may directly trigger inflammatory processes and the release of cytokines, which gain access to the central nervous system. Microglial activation triggers the production of further inflammatory cytokines, oxidative stress via reactive oxygen species (ROS), complement activation, and proteinase generation, eventually leading to neuroinflammation and neuronal cell death.

Animal studies support the role of neuroinflammation and oxidative stress in air pollution-mediated hazard to the central nervous system.^[14] Compared to controls, levels of inflammatory biomarkers, including interleukin-1 (IL-1) and tumor necrosis factor alpha (TNF- α), were reported to be increased in the murine model exposed to airborne particulate matter.^[15] Acute neurobehavioral neurotoxicity could be induced due to oxidative stress, mediated by exposure to benzo (a) pyrene in another rat model.^[16] Reduction in synaptic function after exposure to nanosized particulate matter in the hippocampus may be another potential pathway for brain dysfunction.^[17]

Although precise mechanisms by which air pollution may lead to headaches remain unspecified, there may be several putative mechanisms [Figure 1]. Chemical irritation of trigeminal sensory endings may precipitate headaches, by activating the trigeminovascular system.^[18] Chronic environmental irritant exposure was observed to lead to trigeminovascular system sensitization in male rodent model, probably contributing to enhancement of headache susceptibility.^[19] Male rats were exposed to either acrolein or room air for 4 days. Acrolein is a transient receptor potential ankyrin 1 (TRPA1) agonist. Meningeal blood flow measurements, performed after 4 days of exposure, demonstrated that exposure to acrolein augmented blood flow, in comparison with air exposure. Similarly, chronic environmental irritant exposure was shown to induce a chronic migraine phenotype in a male rat model.^[20] Further support also garners from the syndrome of multiple chemical sensitivity (MCS), in which headache features prominent symptomatic role. MCS displays increased sensitivity to several chemicals, which are TRPA1 agonists.^[21]

The dominant theory of migraine pathophysiology is based on neurogenic inflammation. Substance *P* and calcitonin gene-related peptide (CGRP) release of trigeminal sensory nerve endings produce neurogenic inflammation and dural vasodilatation. Migraine is characterized by increased neuronal sensitivity to a wide range of stimuli. Air pollutants may act as triggers, activating the trigemino-vascular system, and precipitating migraine, possibly in genetically susceptible individuals. PM_{2.5} may activate the sympathetic nervous system, which modulates the trigemino-vascular system in migraine.

Air pollution and migraine

The literature examining the association between air pollution and migraine is sparse, although data on the association

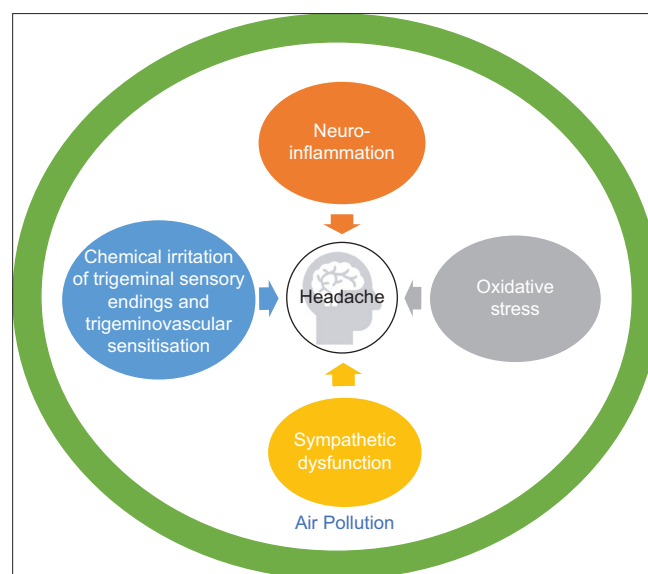


Figure 1: Putative mechanisms interlinking air pollution and headache disorders

between air pollution and neurological disorders are accruing. We have summarized some important points below:

Migraine triggers

Among the most common triggers for migraine include stress, sleep disruption, menstrual changes, pregnancy, dietary triggers, alcohol, and fatigue.^[22,23] Other factors that may trigger migraine include change in weather and environmental noise.^[24] Among migraineurs, there may be a subgroup that is sensitive to weather changes, specifically higher relative humidity during warmer months (April to September).^[25,26]

Certain air pollutants, when exposed to on a short-term basis, have been implicated as triggering factors for migraine. Particulate matter (PM_{2.5}) has been associated with increased visits to the emergency department (ED), due to precipitation of migraine. Increased ED visits specific to migraine have been reported from Canada, Taiwan, and South Korea.^[27-31] Apart from PM_{2.5}, other pollutants implicated include sulfur dioxide (SO₂),^[32] coarse particulate matter (PM₁₀), carbon monoxide, nitrogen dioxide, and ozone, which have been reported from Taiwan.^[30,31] Unconventional natural gas has also been associated with increased migraine headaches.^[33]

Air pollution as a risk factor for migraine

Studies that have examined whether ambient air pollution is a risk factor for migraine have yielded mixed results. A study from Edmonton, Canada, demonstrated increased risk of migraine with ambient air pollution.^[27] In this linear mixed models study, PM_{2.5} during cold weather, PM₁₀ during cold weather among women, and SO₂ during the warm season were associated with increased ED visits for migraine. On the contrary, another study from Boston, USA, did not support the findings of the Canadian study.^[34] This was a case-crossover study. Another study from Taipei, Taiwan, which was a case-crossover study, a significant association was observed between higher levels of air pollution and increased ED visits for migraine.^[31] In a time-stratified, case-crossover study, short-term exposure to high levels of PM_{2.5}, PM₁₀, CO, NO₂, and O₃ correlated with increased ED visits for migraine.^[29]

Effects of individual air pollutants

While the study by Szyszkowicz *et al.*^[27] found an association with PM_{2.5} in the cold season with migraine, the study by Lee *et al.*^[29] found the association in warmer weather. The World Health Organization (WHO) guidelines for air quality recommend annual average PM_{2.5} concentration of 10 µg/m³–25 µg/m³ for 24 hours average. In many regions, including Eastern/Southeast Asia and the Middle East, these recommended levels are superseded. The concentration of PM_{2.5} is relatively higher during cold-passage weather.^[35] The study by Lee *et al.* also observed a significant association with all pollutants except SO₂, whereas Szyszkowicz *et al.* and Chiu *et al.*^[31] observed an association between SO₂ and migraine. In another time-series study, conducted at Vancouver, Canada, increased SO₂ levels were associated with an increased risk for migraine.^[32] There has been debate whether SO₂ per se acts as a harmful air pollutant, or as a surrogate marker

for ultrafine particles.^[36] In the study by Lee *et al.*^[29], the association was strongest for NO₂. NO₂ level, which is a marker of combustion-related pollution, may reflect traffic emissions. In another study among schools in Malaysia, the association between volatile organic compounds (VOCs) and various symptoms among students were assessed. Benzaldehyde was found to be significantly associated with headache.^[37]

The differences in various studies observed above may be due to several reasons. These include regional variations in the composition and proportion of various air pollutants, based on local industrial and traffic emissions, temperature differences, and even interpopulation differences. Moreover, these studies were heterogeneous in many ways, including study design, outcome assessment, and adjustment for confounding factors, which may account for the discrepancies observed.

Long-term exposure

Most of the studies discussed so far have examined the short-term effects of air pollution in terms of migraine-specific ED visits. Data on the ramifications of long-term exposure are sparse but suggest that chronic exposure may be crucial in the etio-pathogenesis of headache disorders, including migraine.

In a case-control study, increased odds of exposure to NO₂ and methane super-emitters were observed among patients with migraine, compared to population controls without migraine. Interestingly, in this study, migraine severity was assessed more comprehensively, in terms of frequency of prescriptions for triptans, migraine-specific ED and outpatient visits, and migraine probability algorithm (MPA) scores. Migraine severity was linked to PM_{2.5} and NO₂ exposure.

In a nationwide Taiwanese study, data were extracted from the Taiwan National Health Insurance Research database and linked to Taiwan Air Quality Monitoring database.^[38] Recurrent headaches in the pediatric age-group were associated with high levels of several air pollutants, including NO₂, PM_{2.5}, methane, and total hydrocarbons, providing links between chronic exposure and headache development.

In a cross-sectional study conducted in Lagos, Nigeria, which was based in a community living adjacent to an open landfill, the health effects of chronic exposure to municipal solid waste fires were examined.^[39] Municipal solid waste burning leads to emissions of multiple air pollutants, including PM, PAH, and several organic pollutants, leading to increased odds for daily occurrence of headaches, apart from multiple other health complaints.

Other headache disorders

In a Chilean time-series analysis conducted between 2001 and 2005, the association between air pollution and hospitalization for headaches was assessed.^[40] Air pollution was found to be associated with three headache subtypes—migraine, headache with cause specified, and headache not otherwise specified.

Biomass fuel

The use of biomass fuel, which is a major source of cooking in several parts of the world, forms a crucial source of indoor air

pollution and is a major cause of morbidity and mortality.^[41] It is believed to lead to 1.6 million premature deaths globally. The burden of this mainly falls on low- and middle-income countries. Cookstove emissions contain several hazardous components, including PM_{2.5}, CO, NO₂, and multiple organic compounds.

In a cross-sectional study from Honduras, the odds of prevalent headache was higher among women who used traditional stoves, compared to clean-burning stoves.^[42] Similar observations have also been made in India.^[43,44] In a randomized trial among Mayan Guatemalan women, the odds of having headache and soreness of eyes was significantly reduced by the use of improved stoves (*planchas*), compared to groups using open fires.^[45] Similar observations have been made in a randomized trial in rural Mexico, in which women were randomized to receive either the (clean-burning) Patsari stove or open fire. Women who used the Patsari stove had lower risk of both respiratory symptoms and headache.^[46] A cross-sectional Peruvian study demonstrated reduced headache in the chimney-equipped stoves, compared to open-fire stoves.^[47]

Haze events

A haze event is a condition characterized by visibility below 10 km and relative humidity below 90%. It is usually caused by fine PM. In a continuous and severe haze event in China in 2013, an increase in emergency calls was noted for several central nervous system conditions, including headache.^[48] Widespread forest fires in Indonesia in 2013 led to severe haze conditions in adjacent countries, leading to an increase in headache symptoms.^[49]

Air pollution and headache: Indian context

Air pollution in India is a rapidly escalating health concern. In 2019, India was home to 21 of the 30 most polluted cities worldwide and 13 of 20 cities in the world with the highest levels of air pollution. In 2019, 1.67 million deaths (95% uncertainty interval 1.42–1.92) could be attributed to air pollution in India.^[50] Most of these deaths were due to ambient PM and household air pollution. Air pollution was also observed to wield enormous economic burden, with an annual loss of US dollar (USD) 28.8 billion from premature deaths and USD 8 million from morbidity attributable to air pollution.^[50]

The main sources of ambient air pollution include biomass fuel combustion, industrial emissions, coal burning, stubble burning, brick kilns, waste burning, vehicular emissions, building construction, and diesel generators. Household air pollution is generated by combustion of solid fuels, including wood, coal, charcoal, etc., which is a common means of cooking food in households across India. Studies from India have demonstrated that short-term chronic air pollution leads to increased morbidity and mortality.^[51,52] However, limited literature exists on the impact of air pollution on headache disorders [Table 1]. In a cross-sectional study from Cuttack, Odisha, exposure to biomass fuel smoke was significantly associated with headache, along with dry cough

and hypertension.^[43] In another study from Lucknow, Uttar Pradesh, indoor air pollution correlated with symptoms of headache, depression, bronchial asthma, and dizziness.^[53] An exposure–response study from Nagpur, Maharashtra, observed that symptoms of ocular irritation, headache, and visual diminution were significantly higher among users of biomass fuel.^[44] In a study from Gwalior, India, among traffic police persons, headache was among the most frequently reported symptoms in association with air pollution.^[54]

Future directions and mitigative strategies

It is apparent from the above discussion that there is a broad avenue and opportunity for further research exploring the relationship between air pollution and headache disorders.

Most studies examining the relationship between ambient air pollution and migraine have employed migraine-specific ED visits, as a proxy marker of severe headache. This is a crude marker and gives no indication of actual severity. Moreover, it underrepresents individuals who may have moderate-to-severe headache but self-medicate at home. Hence, better outcome assessment tools need to be designed to assess the true effects of air pollution on migraine and other headache disorders. Assessing the role of genetic influences in the interaction between headaches and air pollution should be explored further, to understand which headache subpopulations are susceptible to the ill effects of pollution.

Furthermore, studies must be planned in a uniform way, with stringent outcome assessment, and statistical analysis stringently adjusted for confounding factors, such as holidays, sunlight hours, and the like, to avoid heterogeneous assessment of the impact of pollution variables on headache parameters. Also, since air pollution is highly determined by local factors, indigenous studies must be planned to assess the risk of air pollution for worsening/exacerbation of headache disorders in our population.

It is also apparent that there is an urgent need to plan and execute efficient mitigating strategies to attenuate the scourge of air pollution, not only in terms of headache disorders, but also for overall health and well-being. Solutions may include the use of more energy-efficient fuel sources, alternative energy methods such as hydroelectric and solar energy, and the use of electric vehicles. There also need to be long-term solutions to contemporary regional issues such as stubble burning, industrial emissions, and biomass fuel usage.

CONCLUSIONS

Air pollution is rapidly becoming a major environmental health risk factor, with Southeast Asia being the most polluted region worldwide. It has been associated with several neurological disorders, including neurodegenerative disorders, including Alzheimer's disease, Parkinson's disease, psychological disorders, stroke, developmental disorders, etc., Multiple subcomponent pollutants are responsible for adverse health effects, including increased association with occurrence of

Table 1: Studies from India assessing the association between air pollution and headache disorders

Author, year of publication	Study design	Methods	Outcomes
Mohapatra <i>et al.</i> , 2018 ^[43]	Cross section study	Location: Cuttack, Odisha Aim: To assess association between cooking fuel usage and self-reported symptoms	Headache significantly associated with the number of cooking years
Sukhsohale <i>et al.</i> , 2013 ^[44]	House-to-house survey	Location: Nagpur, Maharashtra Aim: To assess the association between cooking fuel use and various morbidities	Headache was significantly associated with the use of biomass fuel
Lawrence <i>et al.</i> , 2014 ^[53]	Survey	Location: Lucknow, Uttar Pradesh Aim: Association between indoor air pollution and symptoms assessed	Headache among the most frequent symptoms reported from polluted regions
Sharma <i>et al.</i> , 2017 ^[54]	Questionnaire survey	Location: Gwalior, Madhya Pradesh Aim: Assess perceived health effects of air pollution on traffic police persons	Headache was reported among many symptoms by traffic police persons

headache disorders, including migraine. These include PM, NO₂, SO₂, and the like. While there are accumulating data on the association between air pollution and headaches overall, and migraine specifically, there are several gaps in our understanding of pathophysiology and possible therapeutic avenues. Future efforts should focus on these gaps, and region-specific efforts must be made to capture the full extent of the effect of air pollution on headache disorders.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: A systematic analysis for the Global burden of disease study 2019. *Lancet* 2020;396:1204-22.
- Steiner TJ, Stovner LJ, Jensen R, Uluduz D, Katsarava Z. Migraine remains second among the world's causes of disability, and first among young women: Findings from GBD2019. *J Headache Pain* 2020;21:137.
- Friedman DI, De ver Dye T. Migraine and the environment. *Headache* 2009;49:941-52.
- Manisalidis I, Stavropoulou E, Stavropoulos A, Bezirtzoglou E. Environmental and health impacts of air pollution: A review. *Front Public Health* 2020;8:14.
- New WHO Global Air Quality Guidelines aim to save millions of lives from air pollution. <https://www.who.int/news/item/22-09-2021-new-who-global-air-quality-guidelines-aim-to-save-millions-of-lives-from-air-pollution>. [Last accessed on 2021 Dec 19].
- Lim YH, Kim H, Kim JH, Bae S, Park HY, Hong YC. Air pollution and symptoms of depression in elderly adults. *Environ Health Perspect* 2012;120:1023-8.
- Kim SY, Kim JH, Kim YH, Wee JH, Min C, Han S-M, *et al.* Short- and long-term exposure to air pollution increases the risk of stroke. *Int J Stroke* 2021;17474930211042118. doi: 10.1177/17474930211042118. Online ahead of print.
- Elgabsi M, Novack L, Yarza S, Elgabsi M, Shtein A, Ifergane G. An impact of air pollution on moderate to severe relapses among multiple sclerosis patients. *Mult Scler Relat Disord* 2021;53:103043.
- Jo S, Kim Y-J, Park KW, Hwang YS, Lee SH, Kim BJ, *et al.* Association of NO₂ and other air pollution exposures with the risk of Parkinson disease. *JAMA Neurol* 2021;78:800-8.
- Lotfi F, Mansourian M, Mirmoayyeb O, Najdaghi S, Shaygannejad V, Esmail N. Association of exposure to particulate matters and multiple sclerosis: A systematic review and meta-analysis. *Neuroimmunomodulation* 2021;196-202. doi: 10.1159/000516559. Online ahead of print.
- Mortamais M, Gutierrez LA, de Hoogh K, Chen J, Vienneau D, Carrière I, *et al.* Long-term exposure to ambient air pollution and risk of dementia: Results of the prospective three-city study. *Environ Int* 2021;148:106376.
- Farahmandfard MA, Naghibzadeh-Tahami A, Khanjani N. Ambient air pollution and multiple sclerosis: A systematic review. *Rev Environ Health* 2021;36:535-44.
- Block ML, Calderón-Garcidueñas L. Air pollution: Mechanisms of neuroinflammation and CNS disease. *Trends Neurosci* 2009;32:506-16.
- Mills NL, Donaldson K, Hadoke PW, Boon NA, MacNee W, Cassee FR, *et al.* Adverse cardiovascular effects of air pollution. *Nat Clin Pract Cardiovasc Med* 2009;6:36-44.
- Campbell A, Oldham M, Becaria A, Bondy SC, Meacher D, Sioutas C, *et al.* Particulate matter in polluted air may increase biomarkers of inflammation in mouse brain. *Neurotoxicology* 2005;26:133-40.
- Saunders CR, Das SK, Ramesh A, Shockley DC, Mukherjee S. Benzo (a) pyrene-induced acute neurotoxicity in the F-344 rat: Role of oxidative stress. *J Appl Toxicol* 2006;26:427-38.
- Davis DA, Akopian G, Walsh JP, Sioutas C, Morgan TE, Finch CE. Urban air pollutants reduce synaptic function of CA1 neurons via an NMDA/NO pathway in vitro. *J Neurochem* 2013;127:509-19.
- Kunkler PE, Ballard CJ, Pellman JJ, Zhang L, Oxford GS, Hurley JH. Intraganglionic signaling as a novel nasal-meningeal pathway for TRPA1-dependent trigeminovascular activation by inhaled environmental irritants. *PLoS One* 2014;9:e103086.
- Kunkler PE, Zhang L, Pellman JJ, Oxford GS, Hurley JH. Sensitization of the trigeminovascular system following environmental irritant exposure. *Cephalalgia* 2015;35:1192-201.
- Kunkler PE, Zhang L, Johnson PL, Oxford GS, Hurley JH. Induction of chronic migraine phenotypes in a rat model after environmental irritant exposure. *Pain* 2018;159:540-9.
- Cullen MR. The worker with multiple chemical sensitivities: An overview. *Occup Med* 1987;2:655-61.
- Peroutka SJ. What turns on a migraine? A systematic review of migraine precipitating factors. *Curr Pain Headache Rep* 2014;18:454.
- Hindiyeh NA, Zhang N, Farrar M, Banerjee P, Lombard L, Aurora SK. The role of diet and nutrition in migraine triggers and treatment: A systematic literature review. *Headache* 2020;60:1300-16.
- Li W, Bertisch SM, Mostofsky E, Buettner C, Mittleman MA. Weather, ambient air pollution, and risk of migraine headache onset among

- patients with migraine. *Environ Int* 2019;132:105100.
25. Yang AC, Fuh JL, Huang NE, Shia BC, Wang SJ. Patients with migraine are right about their perception of temperature as a trigger: Time series analysis of headache diary data. *J Headache Pain* 2015;16:49.
 26. Hoffmann J, Lo H, Neeb L, Martus P, Reuter U. Weather sensitivity in migraineurs. *J Neurol* 2011;258:596-602.
 27. Szyszkowicz M, Stieb DM, Rowe BH. Air pollution and daily ED visits for migraine and headache in Edmonton, Canada. *Am J Emerg Med* 2009;27:391-6.
 28. Szyszkowicz M, Kaplan GG, Grafstein E, Rowe BH. Emergency department visits for migraine and headache: A multi-city study. *Int J Occup Med Environ Health* 2009;22:235-42.
 29. Lee H, Myung W, Cheong H-K, Yi S-M, Hong Y-C, Cho S-I, *et al.* Ambient air pollution exposure and risk of migraine: Synergistic effect with high temperature. *Environ Int* 2018;121:383-91.
 30. Chang CC, Chiu HF, Yang CY. Fine particulate air pollution and outpatient department visits for headache in Taipei, Taiwan. *J Toxicol Environ Health A* 2015;78:506-15.
 31. Chiu HF, Weng YH, Chiu YW, Yang CY. Air pollution and daily clinic visits for headache in a subtropical city: Taipei, Taiwan. *Int J Environ Res Public Health* 2015;12:2277-88.
 32. Szyszkowicz M, Rowe BH, Kaplan GG. Ambient sulphur dioxide exposure and emergency department visits for migraine in Vancouver, Canada. *Int J Occup Med Environ Health* 2009;22:7-12.
 33. Tustin AW, Hirsch AG, Rasmussen SG, Casey JA, Bandeen-Roche K, Schwartz BS. Associations between unconventional natural gas development and nasal and sinus, migraine headache, and fatigue symptoms in Pennsylvania. *Environ Health Perspect* 2017;125:189-97.
 34. Mukamal KJ, Wellenius GA, Suh HH, Mittleman MA. Weather and air pollution as triggers of severe headaches. *Neurology* 2009;72:922-7.
 35. Feng X, Wang S. Influence of different weather events on concentrations of particulate matter with different sizes in Lanzhou, China. *J Environ Sci (China)* 2012;24:665-74.
 36. World Health Organization. Air Quality Guidelines: Global Update 2005: Particulate Matter, Ozone, Nitrogen Dioxide, and Sulfur Dioxide. World Health Organization; Geneva, Switzerland. 2006.
 37. Norbäck D, Hashim JH, Hashim Z, Ali F. Volatile organic compounds (VOC), formaldehyde and nitrogen dioxide (NO₂) in schools in Johor Bahru, Malaysia: Associations with rhinitis, ocular, throat and dermal symptoms, headache and fatigue. *Sci Total Environ* 2017;592:153-60.
 38. Hong SY, Wan L, Lin HJ, Lin CL, Wei CC. Long-term ambient air pollutant exposure and risk of recurrent headache in children: A 12-year cohort study. *Int J Environ Res Public Health* 2020;17:E9140.
 39. Adetona O, Ozoh OB, Oluseyi T, Uzoegwu Q, Odei J, Lucas M. An exploratory evaluation of the potential pulmonary, neurological and other health effects of chronic exposure to emissions from municipal solid waste fires at a large dumpsite in Olusosun, Lagos, Nigeria. *Environ Sci Pollut Res Int* 2020;27:30885-92.
 40. Dales RE, Cakmak S, Vidal CB. Air pollution and hospitalization for headache in Chile. *Am J Epidemiol* 2009;170:1057-66.
 41. GBD 2016 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2016: A systematic analysis for the Global Burden of disease study 2016. *Lancet* 2017;390:1345-422.
 42. Walker ES, Clark ML, Young BN, Rajkumar S, Benka-Coker ML, Bachand AM, *et al.* Exposure to household air pollution from biomass cookstoves and self-reported symptoms among women in rural Honduras. *Int J Environ Health Res* 2020;30:160-73.
 43. Mohapatra I, Das SC, Samantaray S. Health impact on women using solid cooking fuels in rural area of Cuttack district, Odisha. *J Family Med Prim Care* 2018;7:11-5.
 44. Sukhsohale ND, Narlawar UW, Phatak MS. Indoor air pollution from biomass combustion and its adverse health effects in central India: An exposure-response study. *Indian J Community Med* 2013;38:162-7.
 45. Diaz E, Smith-Sivertsen T, Pope D, Lie RT, Díaz A, McCracken J, *et al.* Eye discomfort, headache and back pain among Mayan Guatemalan women taking part in a randomised stove intervention trial. *J Epidemiol Community Health* 2007;61:74-9.
 46. Romieu I, Riojas-Rodríguez H, Marrón-Mares AT, Schilman A, Perez-Padilla R, Masera O. Improved biomass stove intervention in rural Mexico: Impact on the respiratory health of women. *Am J Respir Crit Care Med* 2009;180:649-56.
 47. Li Z, Commodore A, Hartinger S, Lewin M, Sjödin A, Pittman E, *et al.* Biomonitoring human exposure to household air pollution and association with self-reported health symptoms-A stove intervention study in Peru. *Environ Int* 2016;97:195-203.
 48. Cui L, Conway GA, Jin L, Zhou J, Zhang J, Li X, *et al.* Increase in medical emergency calls and calls for central nervous system symptoms during a severe air pollution event, January 2013, Jinan City, China. *Epidemiology* 2017;28(Suppl 1):S67-73.
 49. Ho RC, Zhang MW, Ho CS, Pan F, Lu Y, Sharma VK. Impact of 2013 South Asian haze crisis: Study of physical and psychological symptoms and perceived dangerousness of pollution level. *BMC Psychiatry* 2014;14:81.
 50. India State-Level Disease Burden Initiative Air Pollution Collaborators. Health and economic impact of air pollution in the states of India: The Global Burden of disease study 2019. *Lancet Planet Health* 2021;5:e25-38.
 51. Prabhakaran D, Mandal S, Krishna B, Magsumbol M, Singh K, Tandon N, *et al.* Exposure to particulate matter is associated with elevated blood pressure and incident hypertension in Urban India. *Hypertension* 2020;76:1289-98.
 52. Siddique S, Ray MR, Lahiri T. Effects of air pollution on the respiratory health of children: A study in the capital city of India. *Air Qual Atmos Health* 2011;4:95-102.
 53. Lawrence A, Fatima N. Urban air pollution and its assessment in Lucknow City--The second largest city of North India. *Sci Total Environ* 2014;488-489:447-55.
 54. Sharma HK, Dandotiya B, Jadon N. Exposure of air pollution and its health effects in traffic police persons of Gwalior City, India. *Environ Claims J* 2017;29:305-15.