Review Article

Air Pollution and Cerebrovascular Disorders with Special Reference to Asia: An Overview

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Abstract

Background: Among the primary environmental issues affecting global health, air pollution is considered the leading cause of concern. Globally, around 800,000 deaths were attributed to air pollution according to WHO. Evidence suggests that there has been a strong association of air pollution with stroke. Approximately, 25% of stroke mortality was due to air pollution according to a study in 2013. **Objective:** The aim of this review was to analyze the association between stroke, intracerebral hemorrhage, and subarachnoid hemorrhage and air pollution and its burden globally with a special focus on South Asia along with its association with the COVID-19 pandemic. **Results:** There is growing research data linking air pollution to cardiovascular disorders including stroke. Short-term and long-term air pollution exposures have been shown to increase stroke incidence in epidemiological data. Air pollution, both gaseous and particle, show a strong and tight temporal relationship with stroke hospitalizations and death. The link between ICH and SAH to air pollution is less strong and less well studied as compared to ischemic stroke. Stroke and air pollution both are highly prevalent in South Asia. It is possible that the high prevalence of stroke in south Asia may be linked to the high frequency of air pollution in addition to other conventional risk factors. Decreased stroke admissions and mortality and reduced cardiovascular mortality reported during coronavirus disease 2019 (COVID) lockdown may be attributable to decreased levels of air pollution. **Conclusion:** Even though air pollution poses a significant threat to human health, a great number of countries still fail to achieve internationally agreed air quality standards. Air pollution should be recognized among the most significant controllable risk factors for cardiovascular and cerebrovascular disease prevention and treatment.

Keywords: Air pollution, burden, COVID-19, particulate matter, South Asia, stroke

Introduction

Air pollution is a serious global issue and is considered one of the chief environmental exposures responsible for morbidity and mortality. As concluded by the Lancet commission about health and pollution, it is the world's leading environmental cause of premature deaths and disease today, accounting for an estimated 16% of all fatalities and linked to a considerably broader spectrum of diseases than previously assumed.[1] According to the World Health Organization, particulate matter bearing diameter of approximately 2.5 mm (PM2.5) causes roughly 800,000 deaths each year globally, accounting for 40% of mortality attributable to outdoor air pollution.[2] Several epidemiologists have confirmed links between extended exposure to air pollution and the occurrence of cardiovascular disease leading to death.[3] Varied biological pathways influencing the cardiovascular system as well as the progression of atherosclerosis have been linked to air pollution, which include systemic inflammation, autonomic nervous system imbalance, and oxidative stress, all of which are recognized mechanisms of disease contributing to stroke or cardiovascular disease.[4]

Stroke is among the leading public health problems. In 2019, incident cases of strokes accounted for 12.2 million, prevalent cases accounted for 101 million, stroke-related DALYs accounted for 143 million, and 6.55 million deaths were attributed to stroke. Worldwide, stroke was the second leading cause of death (11.6%of total deaths) and the third leading cause of death and disability combined (5.7% of total DALYs) in 2019.[5] Stroke is projected to become more common in the future, particularly in countries with a significantly older population.[6] Air pollution is responsible for even more than 25% of stroke incidence and mortality, as per the Global Burden of Disease Study of 2013. In contrast to well-known factors associated with ischemic strokes, such as smoking, poor diet, and physical inactivity, air pollution is a documented controllable risk factor that is independent of changes in an individual's behavior.[7] Over the last two decades, high-income countries witnessed a prominent drop in DALYs related to stroke by 20% to 40%.[7,8] At the same time, the majority of strokes (85% approximately) occurred

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in LMICs.[8] Air pollution is expected to rise dramatically in LMICs over the next couple of decades as a result of increased industrialization.[9,10] The objective of this review was to analyze the association of stroke and air pollution and its burden, especially in South Asia along with its association with COVID-19 pandemic.

Methods

We searched databases including Embase, Medline (PubMed), and Web of Science. Additional filters included the English language, published between December 2000 and December 2021. The keywords of interest for the title were: stroke, cerebrovascular events, intracerebral hemorrhage, subarachnoid hemorrhage, mortality, cognitive decline, COVID-19, air pollution, and air pollutants. There was no preference for study design. Our search included literature reviews, cohort studies, editorials, and stroke registries. We retrieved 59 articles of which46 were included in our literature review. Stroke registries,[3] case-control and cohort studies,[11] systematic reviews and literature reviews,[12] and editorials[3] were included.

Air pollution

Air pollution is a broad word terminology that refers to a dynamic combination of millions of molecules originating from a variety of diverse sources. Air pollution is any biological, physical, or chemical factor that contaminates the outdoor and indoor environment and alters the natural elements of the atmosphere. Air pollution is commonly caused by domestic combustion appliances, automobiles, industrial plants, and wildfires. Pollutants of major concern include particulate matter, oxides of carbon, nitrogen, sulfur, and ozone.[13]

Particulate matter

Particulate matter is composed of relatively minute particles and droplets of acids, organic compounds, metals, and dust or soil particles. It is a fraction of air pollution but is a significant contributor to human health and disease. Based on the size of the particles, the airborne particulate matter is categorized into coarse particles possessing a diameter of less than 10 m, fine particles possessing a diameter of less than 2.5 m, and ultrafine or nanoparticles possessing a diameter of less than 0.1 m. The source is usually a determinant of the composition and size of particles. PM10 is mostly emitted into the air because of soil resuspension, construction operations, and industrial effluents. Fine particulate matter is mostly produced by the burning of fossil fuels, such as automobiles, power plants, and commercial and household heating using petroleum, coal, or wood. Transitional metals, nitrates, sulfates, carbon, and complex organic compounds are frequent constituents of these particles.

Even though most of the information for fine particulate matter (PM2.5) is known,[14] there is still some doubt about the shape of the dose-response function, especially at low exposure levels.[15] Some researchers have revealed that the lower range has a sharp slope,[15] whereas others have found a progressive linear association.[3] Only a handful of studies have looked at the long-term impacts of other regulated pollutants such as oxides of nitrogen (NO2) and ozone (O3), as well as pollutants such as black carbon (a soot indicator).[14] Air pollution has been linked to several non-communicable diseases (NCDs), including cardiac disease, cerebrovascular disease, and malignancies.[1]

Gaseous elements of pollution

Oxides of sulfur, nitrogen, carbon, and ozone make up most of the gaseous pollutants. SO2 is mostly produced by fossil-fuel energy plants, whereas nitrogen oxides are primarily produced by motorized traffic, household heating, power production, and industrial emissions. Apart from their intrinsic toxicity, SO2 and nitrogen oxides can play a role in photochemical reactions in the atmosphere, generating complex secondary particles made up of organic and inorganic molecules. Ozone, a type of gaseous contaminant formed when NO2 reacts photochemically with hydrocarbons with high volatility, with catalyst light of the sun, and it is a primary component of photochemical smog.

Epidemiology of stroke and air pollution

Air pollution has become a serious predictor of cardiovascular disease all around the world solely accounting for more than three million fatalities per year.[16] The rise in average pollution concentrations is linked to severe myocardial infarction, hospitalization, and mortality from cardiac arrest.[17] These links might be conferred by direct and indirect effects of air pollution on endothelial function, vascular tone, thrombosis, and myocardial ischemia.[11,18]

Stroke is the cause of five million deaths each year and is the leading etiological component of disability.[19] Stroke is becoming more common, especially in low-income and middle-income nations, where two-thirds of all cerebrovascular accidents occur.[20] The prevalence of stroke has been linked to the aging population in high-income nations and the aggregation of stroke risk factors in low-income and middle-income countries such as obesity, smoking, and hypertension.[21] The effect of environmental variables on stroke morbidity and death, on the other hand, may be significant but is less definite.[22] Acute ischemic stroke and coronary syndrome share air pollution as a significant and modifiable risk factor.[17] Because of its function as a novel modifiable cerebrovascular risk factor, air pollution should be acknowledged as a silent killer that causes stroke and necessitates public health interventions.[23]

Long-term exposure

Extended exposure to pollution raises the risk of cardiac disease, although the health implications of exposure are yet unknown.[12] According to a 2013 meta-analysis, every 10 g/cubic meter rise in PM2.5 was linked to extra risk of 6% for all causes of death and 11% for cardiovascular mortality.[24] Increased hazard ratios for incidence of stroke were found with long-term exposure to PM2.5, black carbon, and NO2, in a pooled analysis of approximately 130,000 individuals from

European cohorts. Only NO2 exposure resulted in an increase in the hazard ratio in patients with coronary heart disease. When curtailing analyses of respondents living in concentrations of pollutants below the EU annual mean limits of 40 g/cubic meter for nitrogen dioxide and 25 g/cubic meter for particulate matter with a diameter less than 2.5 m, the US standard limit of 12 g/cubic meter for PM2.5 and the air quality guideline by WHO, level of 40 g/cubic meter for NO2 and 10 g/cubic meter for PM2, the concentration-response functions revealed visible associations.[12] In LMICs with higher levels of air pollution, interactions with cerebrovascular stroke were shown to be stronger.[25] In a study conducted in China, PM1 and PM2.5 exposure before a stroke was linked to an elevated risk of fatal ischemic stroke in the year after.[26]

Short-term exposure

The risk of the development of intracerebral hemorrhage is increased by short-term air pollution exposure.[27] A 10-microgram per cubic meter increase in PM10 was associated with a rise in admission rates for cardiovascular diseases by 0.8% (95% CI: 0.5-1.2%), ischemic heart diseases by 0.7% (95% CI: 0.4-1.0%), and cerebrovascular injury 0.2% (95% CI: -0.2, 0.6%).[28] In a systematic analysis corresponding to 6.2 million events of stroke in 28 countries, associations were strongly noted on the day of exposure with the most significant results observed for PM2.5. It was concluded that air pollution, both gaseous and particle, show a strong and tight temporal relationship with stroke hospitalizations and death.[29] Pooled estimates depicted associations of higher significance for NO_2 in LMICs than in countries with high income, relative risks of 1.02 as compared to 1.01 was observed, and PM_{10} of 1.004 as compared to 1.002 was observed.[29]

Possible interventions

Even though air pollution poses a significant threat to human health, a great number of countries still fail to achieve internationally agreed air quality standards.[30] Nonetheless, during the last decade, global knowledge of the health implications of air pollution has increased significantly, and the desire for global initiatives to combat air pollution has begun with optimism. Policy reforms at all levels including local, national, regional, and international will be necessary to minimize air pollution and its impact. Fossil fuel combustion is a major contributor to air pollution with well-known health implications. Shifting from fossil fuels toward cleaner and more sustainable energy sources such as wind and solar power might help to minimize not just the negative health consequences of air pollution, similarly, but also contribute to addressing environmental issues such as climate change caused by greenhouse gas emissions.

A variety of easy steps might limit human exposure to air pollution on an individual basis. Commuting using public transportation, cycling, or walking rather than driving a car, limiting time spent outside during particularly unhealthy times, avoiding peak traffic hour, or exercising near major traffic areas are just a few of these approaches. In LMICs, avoiding the application of biomass for residential heating purposes, as well as improving ventilation systems, might have a significant effect. Individuals with a history of pre-existing cardiopulmonary disorders should be informed about the negative effects of air pollution and encouraged to take steps to decrease exposure.[31]

Intracerebral hemorrhage (ICH) and air pollution

Primary ICH occurs as a result of spontaneous rupture of small arteries in the brain and is generally linked with hypertension or cerebral amyloid angiopathy, whereas secondary ICH can originate from vascular abnormalities or tumors.[32] ICH, despite any origin, leads to a significant morbidity and mortality. According to 2013 data, it had a mortality rate of 52.8 per 100,000 people and 1015.6 disability = adjusted life years per 100,000 people globally.[33] Therefore, identifying modifiable risk factors and addressing these with public health intervention is very critical to lowering down its prevalence.[34]

There is evidence that there is a link between ambient air pollutants and the occurrence of ICH with the greatest connections being observed for particulate matter of an aerodynamic diameter of 2.5 m (PM2.5) and 10 m (PM10) and Nitrogen oxide (NO2).[35,36] In Taiwan, a link between NO2 level and prevalence of spontaneous ICH in people of all ages was found.[35,37] However, they were not able to demonstrate the association regarding seasonal and temporal changes.[35] The seasonal fluctuations were considered by a study and identified a link between PM10 and NO2 and ICH on hot days.[38] Furthermore, a link between current day NO2 levels and hospital admission for ICH was found in a study[39] whereas another study found that CO exposure in Edmonton, Canada was linked to an elevated risk of ICH.[40]

Long-term exposure to NO2 was related to an elevated risk of ICH in a 9-year cohort study by Yorifuji *et al.* in Japan in 2013.[38] The long-term implication of air pollution for ICH are poorly understood and more prospective longitudinal studies are needed.

Several mechanisms could explain the link between air pollution and ICH. A relationship between air pollution and hypertension has been highlighted in recent systematic reviews and meta-analyses. Yang *et al.* also identified a significant link between short- and long-term exposure to PM10, PM2.5, SO2, and NO2 and hypertension.[39] Chen *et al.* investigated the link between long-term exposure to PM2.5 and incident hypertension in 35,303 non-hypertensive individuals from Ontario, Canada, during a 7.3-year period.[40] These studies show that exposure to air pollution can raise the incidence of hypertension, particularly in people who already have predisposing risk factors.

Long-term exposure to PM2.5 and PM10 in rats resulted in damaging the vascular endothelium and vasodilation. These changes in vascular endothelium may play a role in cerebral aneurysms. Endothelial dysfunction has also been linked to

aneurysm formation and rupture in humans. A prospective longitudinal investigation in humans found that greater PM2.5 levels were linked to higher indicators of systemic inflammation and endothelial cell death. This might be one way by which air pollution increases the risk of ICH.

Several studies on the other hand found no significant links between air pollution. Hong *et al.* in south Korea in a longitudinal research and Tian *et al.* discovered no link between air pollution and ICH.[41]

Existing worldwide research on the link between ambient air pollution and the risk of ICH offers significant evidence. More studies are needed to look at the long-term impacts of air pollution on ICH risk and to investigate the pathophysiological processes through which air pollution can be linked to an elevated risk of ICH.

Sub arachnoid hemorrhage (SAH) and air pollution

Currently, stroke is the leading cause of morbidity and mortality worldwide and environmental factors play a strong causative role in stroke, out of which subarachnoid hemorrhage is found to be related to atmospheric risk factors such as air contamination, barometric pressure, and extreme climate change. All these variables contribute to affecting the blood-brain barrier which results in subarachnoid hemorrhage.

An observational cohort study done in Netherland in the years 2000 and 2015 concluded that there was an evident association between variation in air pressure and sub-arachnoid hemorrhage.[42] It is essential to comprehend the mechanism of changes in the brain vessels due to atmospheric variation. The human brain receives its nutrients along with oxygen through the blood-brain barrier and the equilibrium is maintained by the cerebral vessel plasticity which is extremely sensitive to the pressure of carbon dioxide in the blood, elevation of PaCO2 in the blood can cause disturbance in the blood flow to the brain resulting in increased pressure of cerebral blood flow resulting in leakage and rupture of brain vasculature.[43]

Along with PaCO2, the temperature is also studied to be a confounding variable in SAH; studies show that difference in temperature such as extremes of temperature with humidity plays their part in causing SAH.[44]

Hypertension still remains to be the foremost risk factor of SAH but there are many concepts in evolution to understand the association between air pollution and SAH as it is a medical emergency and now a leading cause of dependency and death.[45]

Burden of air pollution in South Asia

As there is a surge in urbanization and monetary development, air pollution is becoming a matter of utmost worry in South Asian countries including Pakistan, Bangladesh, India, Maldives, Bhutan, Nepal, and Sri Lanka. Consisting of a population of approximately 1.89 billion people, South Asia is a low-income region and is a place of shelter for 50% of the world's poverty-stricken population. One of the major challenges in South Asia includes ecological degradation and with the anticipated rise in industrial movement, and exponential growth in the number of automobiles and inhabitants, the input of each country to the air pollution of the region will rise over time drastically. Among the many, India is the chief consumer of energy, followed by Iran and Pakistan. With growing development and mechanization, air pollution has become a significant cause of apprehension in the region of South Asia. The progress of particulate matter and oxides of nitrogen and sulfur have been intensifying progressively in the past few years.

In China, stroke was the cause of 2.2 million deaths (20.7% of overall deaths). Similarly, in India, 0.7 million deaths were attributed to stroke, accounting for 7.5% of all deaths and denoting the third principal cause of expiries. When compared to other continents, a significant variation was observed in the air pollutants concentrations. Statistics issued by WHO exhibited that average yearly concentrations of PM2·5 varied in different regions in 2016: ranging from less than 10 μg/cubic meter and 25 μg/cubic meter^3 in Russia, Europe, and North America; between 10 μg/cubic meter and 50 μg/cubic meter in Africa, South America, and the Middle East; and between 15 μg/cubic meter to more than 50 μg/cubic meter in Asia.

Air pollution and COVID-19

Globally, there was a diminution in outside air pollution concentration levels during the COVID-19 pandemic due to the worldwide lockdown. This set example promoted an exclusive opportunity to study the reduction in diseases attributed to air pollution and the significance of cleaner air. Earlier studies have already shown a significant reduction in stroke admission patients globally throughout the first wave of the COVID-19 pandemic.[32] This reduction can be owed to patients not opting for the typical remedial help, because of anxiety or due to inadequate access to emergency centers. Concurrently, lowered air pollution might also display a reduced stroke incidence. Recently published data from Pakistan showed decreased admissions and stroke mortality during the COVID lockdown.[46]

Conclusion

There is currently a lot of research that links air pollution to cardiovascular disorders including stroke. Short-term and long-term air pollution exposures have been shown to increase stroke incidence in epidemiological data. Platelet activation, endothelial dysfunction, atherosclerosis, and predisposition for coagulation have all been linked to pathophysiological pathways discovered through controlled trials in humans and experimental investigations. Air pollution should be recognized among the most significant controllable risk factors for cardiovascular and cerebrovascular disease prevention and treatment.

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Conflicts of interest

There are no conflicts of interest.

References

1. Landrigan PJ, Fuller R, Acosta NJR, Adeyi O, Arnold R, Basu NN, *et al*. The Lancet Commission on pollution and health. Lancet 2018;391:462-512.
2. Anderson JO, Thundiyil JG, Stolbach A. Clearing the Air: A review of the effects of particulate matter air pollution on human health. J Med Toxicol 2012;8:166-75.
3. Bai L, Shin S, Burnett RT, Kwong JC, Hystad P, van Donkelaar A, *et al*. Exposure to ambient air pollution and the incidence of congestive heart failure and acute myocardial infarction: A population-based study of 5.1 million Canadian adults living in Ontario. Environ Int 2019;132:105004.
4. Rajagopalan S, Al-Kindi SG, Brook RD. Air pollution and cardiovascular disease: JACC state-of-the-art review. J Am Coll Cardiol 2018;72:2054-70.
5. Feigin VL, Stark BA, Johnson CO, Roth GA, Bisignano C, Abady GG, *et al*. Global, regional, and national burden of stroke and its risk factors, 1990-2019: A systematic analysis for the Global Burden of Disease Study 2019. Lancet Neurol 2021;20:795-820.
6. Liu M, Wu B, Wang WZ, Lee LM, Zhang SH, Kong LZ. Stroke in China: Epidemiology, prevention, and management strategies. Lancet Neurol 2007;6:456-64.
7. Feigin VL, Roth GA, Naghavi M, Parmar P, Krishnamurthi R, Chugh S, *et al*. Global burden of stroke and risk factors in 188 countries, during 1990-2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet Neurol 2016;15:913-24.
8. Global, regional, and national burden of neurological disorders during 1990-2015: A systematic analysis for the Global Burden of Disease Study 2015. Lancet Neurol 2017;16:877-97.
9. Lelieveld J, Evans JS, Fnais M, Giannadaki D, Pozzer A. The contribution of outdoor air pollution sources to premature mortality on a global scale. Nature 2015;525:367-71.
10. Kim AS, Cahill E, Cheng NT. Global stroke belt: Geographic variation in stroke burden worldwide. Stroke 2015;46:3564-70.
11. Lundbäck M, Mills NL, Lucking A, Barath S, Donaldson K, Newby DE, *et al*. Experimental exposure to diesel exhaust increases arterial stiffness in man. Part Fibre Toxicol 2009;6:7.
12. Wolf K, Hoffmann B, Andersen ZJ, Atkinson RW, Bauwelinck M, Bellander T, *et al*. Long-term exposure to low-level ambient air pollution and incidence of stroke and coronary heart disease: A pooled analysis of six European cohorts within the ELAPSE project. Lancet Planet Health 2021;5:e620-32.
13. Organization WH. Air Pollution. Available from: https://www.who.int/health-topics/air-pollution#tab=tab_1.
14. Danesh Yazdi M, Wang Y, Di Q, Zanobetti A, Schwartz J. Long-term exposure to PM (2.5) and ozone and hospital admissions of Medicare participants in the Southeast USA. Environ Int 2019;130:104879.
15. Pinault LL, Weichenthal S, Crouse DL, Brauer M, Erickson A, Donkelaar AV, *et al*. Associations between fine particulate matter and mortality in the 2001 Canadian Census Health and Environment Cohort. Environ Res 2017;159:406-15.
16. Brook RD, Rajagopalan S, Pope CA 3rd, Brook JR, Bhatnagar A, Diez-Roux AV, *et al*. Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. Circulation 2010;121:2331-78.
17. Shah AS, Langrish JP, Nair H, McAllister DA, Hunter AL, Donaldson K, *et al*. Global association of air pollution and heart failure: A systematic review and meta-analysis. Lancet 2013;382:1039-48.
18. Brook RD, Brook JR, Urch B, Vincent R, Rajagopalan S, Silverman F. Inhalation of fine particulate air pollution and ozone causes acute arterial vasoconstriction in healthy adults. Circulation 2002;105:1534-6.
19. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, *et al*. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: A systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2095-128.
20. Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, *et al*. Global and regional burden of stroke during 1990-2010: Findings from the global burden of disease study 2010. Lancet 2014;383:245-54.
21. O'Donnell MJ, Xavier D, Liu L, Zhang H, Chin SL, Rao-Melacini P, *et al*. Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): A case-control study. Lancet 2010;376:112-23.
22. Wellenius GA, Burger MR, Coull BA, Schwartz J, Suh HH, Koutrakis P, *et al*. Ambient air pollution and the risk of acute ischemic stroke. Arch Intern Med 2012;172:229-34.
23. Graber M, Mohr S, Baptiste L, Duloquin G, Blanc-Labarre C, Mariet AS, *et al*. Air pollution and stroke. A new modifiable risk factor is in the air. Rev Neurol (Paris) 2019;175:619-24.
24. Hoek G, Krishnan RM, Beelen R, Peters A, Ostro B, Brunekreef B, *et al*. Long-term air pollution exposure and cardio- respiratory mortality: A review. Environ Health 2013;12:43.
25. Zhang P, Dong G, Sun B, Zhang L, Chen X, Ma N, *et al*. Long-term exposure to ambient air pollution and mortality due to cardiovascular disease and cerebrovascular disease in Shenyang, China. PLoS One 2011;6:e20827.
26. Chen G, Wang A, Li S, Zhao X, Wang Y, Li H, *et al*. Long-term exposure to air pollution and survival after ischemic stroke. Stroke 2019;50:563-70.
27. 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:e542-52.
28. Morris RD. Airborne particulates and hospital admissions for cardiovascular disease: A quantitative review of the evidence. Environ Health Perspect 2001;109(Suppl 4):495-500.
29. Shah AS, Lee KK, McAllister DA, Hunter A, Nair H, Whiteley W, *et al*. Short term exposure to air pollution and stroke: Systematic review and meta-analysis. BMJ 2015;350:h1295.
30. Organization WH. WHO Global Urban Ambient Air Pollution Database (update 2016) 2016. 2016. Available from: http://www.who.int/phe/health_topics/outdoorair/databases/cities/en/. [Last accessed on 31 Dec 2021].
31. Lee KK, Miller MR, Shah ASV. Air Pollution and Stroke. J Stroke 2018;20:2-11.
32. Caceres JA, Goldstein JN. Intracranial hemorrhage. Emerg Med Clin North Am 2012;30:771-94.
33. Feigin VL, Krishnamurthi RV, Parmar P, Norrving B, Mensah GA, Bennett DA, *et al*. Update on the Global Burden of Ischemic and Hemorrhagic Stroke in 1990-2013: The GBD 2013 Study. Neuroepidemiology 2015;45:161-76.
34. Krishnamurthi RV, Moran AE, Forouzanfar MH, Bennett DA, Mensah GA, Lawes CMM, *et al*. The global burden of hemorrhagic stroke: A summary of findings from the GBD 2010 study. Global Heart 2014;9:101-6.
35. Chien TY, Ting HW, Chan CL, Yang NP, Pan RH, Lai KR, *et al*. Does the short-term effect of air pollution influence the incidence of spontaneous intracerebral hemorrhage in different patient groups? Big data analysis in Taiwan. Int J Environ Res Public Health 2017;14:1547.
36. Han M-H, Yi H-J, Ko Y, Kim Y-S, Lee Y-J. Association between hemorrhagic stroke occurrence and meteorological factors and pollutants. BMC Neurol 2016;16:59.
37. Liu H, Tian Y, Xu Y, Huang Z, Huang C, Hu Y, *et al*. Association between ambient air pollution and hospitalization for ischemic and hemorrhagic stroke in China: A multicity case-crossover study. Environ Pollut 2017;230:234-41.
38. Yorifuji T, Kashima S, Tsuda T, Ishikawa-Takata K, Ohta T, Tsuruta K, *et al*. Long-term exposure to traffic-related air pollution and the risk of death from hemorrhagic stroke and lung cancer in Shizuoka, Japan. Sci Total Environ 2013;443:397-402.
39. Yang BY, Qian Z, Howard SW, Vaughn MG, Fan SJ, Liu KK, *et al*. Global association between ambient air pollution and blood pressure: A systematic review and meta-analysis. Environ Pollut 2018;235:576-88.
40. Chen H, Burnett RT, Kwong JC, Villeneuve PJ, Goldberg MS, Brook RD, *et al*. Spatial association between ambient fine particulate matter and incident hypertension. Circulation 2014;129:562-9.
41. Hong YC, Lee JT, Kim H, Kwon HJ. Air pollution: A new risk factor in ischemic stroke mortality. Stroke 2002;33:2165-9.

42. van Donkelaar CE, Potgieser ARE, Groen H, Foumani M, Abdulrahman H, Sluijter R, *et al*. Atmospheric pressure variation is a delayed trigger for aneurysmal subarachnoid hemorrhage. World Neurosurg 2018;112:e783-90.
43. Babadjouni RM, Hodis DM, Radwanski R, Durazo R, Patel A, Liu Q, *et al*. Clinical effects of air pollution on the central nervous system; A review. J Clin Neurosci 2017;43:16-24.
44. Chen R, Wang C, Meng X, Chen H, Thach TQ, Wong CM, *et al*. Both low and high temperature may increase the risk of stroke mortality. Neurology 2013;81:1064-70.
45. Lian H, Ruan Y, Liang R, Liu X, Fan Z. Short-Term effect of ambient temperature and the risk of stroke: A systematic review and meta-analysis. Int J Environ Res Public Health 2015;12:9068-88.
46. Hameed S, Khan M, Fatmi Z, Wasay M. Exploring the relationship between Air Quality and Ischemic Stroke Admissions during the COVID-19 pandemic. J Stroke Cerebrovasc Dis. 2021;30:105860.