## Air Pollution on Stroke in Shenzhen, China: A Time-Stratified Case Crossover Study Modified by Meteorological Variables

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Abstract : Stroke is the second leading cause of death and a third leading cause of death and disability worldwide in 2019. Given the significant role of environmental factors in stroke development and progression, it is essential to investigate the effect of air pollution on stroke occurrence while considering the modifying effects of meteorological variables. This study aimed to evaluate the association between short-term exposure to air pollution and the incidence of stroke subtypes in Shenzhen, China, and to explore the potential interactions of meteorological factors with air pollutants. The study analyzed data from January 1, 2006, to December 31, 2014, including 88,214 cases of ischemic stroke and 30,433 cases of hemorrhagic stroke among residents of Shenzhen. Using a time-stratified case-crossover design with conditional quasi-Poisson regression, the study estimated the percentage changes in stroke morbidity associated with short-term exposure to nitrogen dioxide (NO<sub>2</sub>), sulfur dioxide (SO<sub>2</sub>), particulate matter less than 10 mm in aerodynamic diameter (PM10), carbon monoxide (CO), and ozone (O<sub>3</sub>). A five-day moving average of air pollution was applied to capture the cumulative effects of air pollution. The estimates were further stratified by sex, age, education level, and season. The additive and multiplicative interaction between air pollutants and meteorologic variables were assessed by the relative excess risk due to interaction (RERI) and adding the interactive term into the main model, respectively. The study found that NO<sub>2</sub> was positively associated with ischemic stroke occurrence throughout the year and in the cold season (November through April), with a stronger effect observed among men. Each 10  $\mu$ g/m<sup>3</sup> increment in the five-day moving average of NO<sub>2</sub> was associated with a 2.38% (95% confidence interval was 1.36% to 3.41%) increase in the risk of ischemic stroke over the whole year and a 3.36% (2.04% to 4.69%) increase in the cold season. The harmful effect of CO on ischemic stroke was observed only in the cold season, with each 1 mg/m<sup>3</sup> increment in the five-day moving average of CO increasing the risk by 12.34% (3.85% to 21.51%). There was no statistically significant additive interaction between individual air pollutants and temperature or relative humidity, as demonstrated by the RERI. The interaction term in the model showed a multiplicative antagonistic effect between NO<sub>2</sub> and temperature (p-value=0.0268). For hemorrhagic stroke, no evidence of the effects of any individual air pollutants was found in the whole population. However, the RERI indicated a statistically additive and multiplicative interaction of temperature on the effects of PM10 and O<sub>3</sub> on hemorrhagic stroke onset. Therefore, the insignificant conclusion should be interpreted with caution. The study suggests that environmental  $NO_2$  and CO might increase the morbidity of ischemic stroke, particularly during the cold season. These findings could help inform policy decisions aimed at reducing air pollution levels to prevent stroke and other health conditions. Additionally, the study provides valuable insights into the interaction between air pollution and meteorological variables, which underscores the need for further research into the complex relationship between environmental factors and health. Keywords : air pollution, meteorological variables, interactive effect, seasonal pattern, stroke

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