Pollution Study 2022, 3(1), 1986.
https://doi.org/10.54517/ps.v3i1.1986

Article

Investigative analysis of the impact of low-level air pollution NO_2 on mortality rates among residents due to cardiovascular and cerebrovascular diseases

Zesheng Che[1], Xiuqing Cui[2], Bin Wang[3], Yanlin Hui[3], Lan Dai[3], Xueqin Cao[1,4], Chunhong Wang[1], Tingming Shi[2,*]

[1] School of Public Health, Wuhan University, Wuhan 430071, China
[2] Hubei Provincial Center for Disease Control and Prevention, Wuhan 430079, China
[3] Enshi City Center for Disease Control and Prevention, Enshi 445000, China
[4] Jianghan District Center for Disease Control and Prevention, Wuhan 430021, China
*** Corresponding author:** Tingming Shi, tmingshi@163.com

CITATION

Che Z, Cui X, Wang B, et al. Investigative analysis of the impact of low-level air pollution NO_2 on mortality rates among residents due to cardiovascular and cerebrovascular diseases. Pollution Study. 2022; 3(1): 1986.
https://doi.org/10.54517/ps.v3i1.1986

ARTICLE INFO

Received: 21 March 2022
Accepted: 12 April 2022
Available online: 22 April 2022

Abstract: Objective: The study aims to assess the influence of low-level atmospheric nitrogen dioxide (NO_2) on the mortality risk associated with cardiovascular and cerebrovascular diseases in Enshi City, with the intention of providing a scientific foundation for identifying sensitive populations and devising population health policies. **Methods:** Data on air pollutant levels, meteorological factors, and mortality rates due to cardiovascular and cerebrovascular diseases among residents of Enshi City were collected from 2015 to 2018. A generalized additive model, based on the Poisson distribution, was employed to analyze the relationship between low-level NO_2 air pollution and the mortality risk for these diseases. Subgroup analyses were conducted based on age, gender, and season. **Results:** The average concentrations of key gaseous pollutants in Enshi City from 2015 to 2018 were as follows: NO_2 (21.40 μg/m^3), sulfur dioxide (SO_2, 9.68 μg/m^3), carbon monoxide (CO, 0.88 mg/m^3), and ozone (O_3, 61.21 μg/m^3). The analysis of the single-pollutant model indicated that for every 1 μg/m^3 increase in NO_2 concentration across the total population, the risk of dying from cardiovascular and cerebrovascular diseases on the same day (lag0) rose by 0.33% (95% CI: −0.06% to 0.72%, $P > 0.05$). Among females, each 1% increase in NO_2 concentration was associated with a 0.92% increase (95% CI: 0.26% to 1.56%, $P < 0.05$) in the risk of mortality from these diseases with a cumulative lag of 1 day (lag01). During the cold season, every 1 μg/m^3 increase in NO_2 concentration was linked to a 0.62% increase (95% CI: 0.12% to 1.12%, $P < 0.05$) in the mortality risk for the entire population on the same day (lag0). The two-pollutant model results showed that even after adjusting for other gaseous pollutants (SO_2, CO, or O_3), the association between NO_2 and the mortality risk from cardiovascular and cerebrovascular diseases persisted for women and the entire population during the cold season. **Conclusion:** In Enshi City, the presence of low NO_2 pollution levels is associated with an elevated risk of cardiovascular and cerebrovascular disease mortality among both women and the general population, particularly during the colder months. It is crucial to prioritize the health safeguarding of vulnerable populations in regions with low pollution and during specific seasonal periods.

Keywords: air pollution; carbon dioxide; cardiovascular and cerebrovascular diseases; risk of death; time series analysis

1. Introduction

Nitrogen dioxide (NO_2) is one of the main air pollutants in China, and its population health hazard effect has attracted more and more attention [1–4]. Tan and

Liu et al. [5] and Liu et al. [6] found that high pollution level NO_2 exposure has a significant impact on the incidence and death of cardiovascular and cerebrovascular diseases. However, there may be differences in the health impact law of air pollutants under different pollution levels, and the research results of Taj et al. [7] and Shan et al. [8] can provide evidence for this. Previous studies on the death risk of no on cardiovascular and cerebrovascular diseases mostly focused on areas with high pollution level, while there were relatively few pathogenic laws of atmospheric NO_2 in areas with low pollution level.

Enshi City is located in Hubei Province, China. The results published in China Ecological Environment Bulletin in recent years show that the air quality of Enshi City is significantly better than that of China's industrial cities and big cities, and belongs to the area with low NO_2 pollution level. Taking Enshi residents as the research object, the study uses time series analysis to explore the law of the impact of low-level atmospheric NO_2 on the death risk of cardiovascular and cerebrovascular diseases, so as to provide a scientific basis for formulating population health policies.

2. Materials and methods

2.1. Data source death data

Derived from the "population death information registration management system of China disease prevention and control information system", the daily deaths of residents in Enshi from cardiovascular and cerebrovascular diseases (ICD 10: I00-I99) data [9,10]. Air pollution data: Obtain the daily concentration data of gaseous air pollutants, including sulfur dioxide (SO_2), NO_2, carbon monoxide (CO) and ozone (O_3), from two independent state-controlled stations in Enshi City (Enshi electric power company and Hubei University for Nationalities). Take the average value of the summary data of each monitoring station, in which O_3 is the average value of 8-hour concentration. Meteorological data: Obtain daily meteorological data from Enshi Meteorological Bureau, including average temperature and average relative humidity.

2.2. Methods

The generalized additive model based on Poisson distribution was used to explore the impact of the concentration change of air pollutant NO_2 on the death risk of cardiovascular and cerebrovascular diseases in Enshi City. First, a single pollutant model is established to control the confounding factors such as day of week effect (Dow), holiday effect (holiday), long-term trend of time (time), daily average temperature (Temp) and daily average relative humidity (Rhum). The specific model is as follows:

$$\text{Log}\ [E(Y_t)] = \alpha + \beta Z_t + ns(\text{time}, df = 7/\text{year}) + ns(\text{temp}, df = 3) + ns(\text{rhum}, df = 2) + \text{DOW} + \text{Holiday}$$

In the model, $E(Y_t)$ is the expected value of the number of deaths on day t; Y_t is the actual number of deaths on the t day of the observation day; β is the regression

coefficient, which represents the relative risk of death from cardiovascular and cerebrovascular diseases related to the increase unit of NO_2 concentration level; Z_t represents the pollutant concentration on the *t* day of the observation day; *ns* is a natural cubic spline function; α is the intercept of the equation; *df* is the degree of freedom of each parameter. The degree of freedom of temp is 3, the degree of freedom of Rhum is 2, and the long-term trend degree of freedom of time is 7. The degree of freedom is determined according to the experience of previous research [11–13] and the minimum principle of Akaike information criterion [14].

There is a lag in the impact of pollutants on people's health, so the lag effect of 4D NO_2 on the incidence of stroke is explored in the study, including one-day lag (lag0–lag4) and cumulative lag (lag01–lag04). Different populations have different sensitivities to air pollutants, so the study is conducted on age (≥65 years old; <65 years old), gender (male; female), season (cold: October to December and January to March; Warm: Subgroup analysis of Liu et al. [15] from April to September. A double pollutant model of NO_2 and other gaseous pollutants is established to explore the impact of adding other gaseous pollutants on the health effect of NO_2.

The results are expressed by excess risk (ER) and 95% confidence interval (CI), where $\mathrm{ER} = \left[e^{\beta} - 1\right] \times 100\%$, which represents the change in the relative percentage of cardiovascular and cerebrovascular death risk of residents per 1 μg/m^3 increase in atmospheric NO_2.

2.3. Statistical analysis

Spearman rank correlation and generalized additive model are used to analyze the correlation between air pollutants and meteorological elements and the impact of air pollutant NO_2 on the death risk of cardiovascular and cerebrovascular diseases. The study used software R 4.0.5. For statistical analysis, and used two-sided test to test the level $\alpha = 0.05$.

3. Results

3.1. Descriptive analysis

The total number of deaths from cardiovascular and cerebrovascular diseases in Enshi City from 1 January 2015 to 31 December 2018 was 6971, of which men and women accounted for 55.47% and 44.53% respectively, people aged ≥65 and <65 accounted for 85.11% and 14.89% respectively, and the deaths in cold season and warm season accounted for 56.78% and 43.22% respectively. In the same period, the average NO_2 concentration in Enshi was 21.40 μg/m^3, the average concentration of other gaseous pollutants is SO_2 (9.68 μg/m), CO (0.88 mg/m), O_3 (61.21 μg/m). The range of daily average temperature is 4.02 ℃~27.40 ℃; the range of daily average relative humidity is 3.44%~97.40% (**Table 1**).

The correlation analysis results of air pollutants and meteorological elements show that the daily average concentration of NO_2 is significantly positively correlated with the daily average concentration of SO_2 (rank correlation coefficient $rs = 0.351$, $P < 0.01$) and CO ($rs = 0.372$, $P < 0.01$), and negatively correlated with O_3 ($rs = 0.398$, $P < 0.01$). Daily average temperature ($rs = 0.516$, $P < 0.01$) and daily

average relative humidity (*rs* = 0.073) were also significantly negatively correlated with NO_2.

Table 1. Descriptive statistics for daily air pollutants, meteorological variables and death of cardiovascular and cerebrovascular diseases in Enshi City from 2015–2018.

Variable	Death toll	Mean ± SD	Minimum value	P_{25}	P_{50}	P_{75}	Maximum
Population characteristics							
Total population	6971	4.77 ± 2.46	0	3	5	6	21
Male	3867	2.65 ± 1.71	0	1	2	4	10
Female sex	3104	2.13 ± 1.53	0	1	2	3	11
≥65 years old	5933	0.71 ± 0.87	0	0	0	1	4
<65 years old	1038	4.06 ± 2.27	0	2	4	5	20
Cold season	3958	5.43 ± 2.59	0	4	5	7	21
Warm season	3013	4.12 ± 2.13	0	3	4	5	12
Atmospheric pollutant							
SO_2 (μg/m^3)		9.68 ± 7.75	1.58	5.83	7.75	11.52	61.68
NO_2 (μg/m^3)		21.40 ± 10.21	3.44	14.34	19.73	27.31	72.94
CO (μg/m^3)		0.88 ± 0.34	0.20	0.64	0.85	1.03	2.53
O_3 (μg/m^3)		61.21 ± 31.51	2.63	38.62	58.94	81.83	184.31
Meteorological factors							
Daily average temperature (*T*)		13.89 ± 7.64	-4.02	6.98	14.57	20.62	27.40
Relative humidity (%)		78.62 ± 9.48	42.71	71.80	79.64	86.74	94.40

3.2. Time series analysis

3.2.1. Single pollutant model and subgroup analysis results

The analysis results of single pollutant model (**Figure 1**) shows that the impact of the increase of daily average concentration of atmospheric NO_2 on the death risk of cardiovascular and cerebrovascular diseases of Enshi residents is not statistically significant in the difference between the time difference of single day lag and cumulative lag, but the difference between the two subgroups in women and cold season is statistically significant Among the female subgroups, there were significant differences in the results of lag0, Lag1, lag01 and lag04 ($P < 0.05$). Among them, the effect value of lag01 was the largest, which was 0.92% (0.26%~1.56%), that is, every increase of NO_2 concentration μg/m^3, the death risk of cardiovascular and cerebrovascular diseases in female population will increase by 0.92% In the subgroup of cold season, only lag0 was observed with statistically significant difference ($P < 0.05$), which was 0.62% (0.12%~1.12%), i.e., every 1% increase in NO_2 concentration μg/m^3, the death risk of cardiovascular and cerebrovascular diseases in the whole population will increase by 0.62% in cold season.

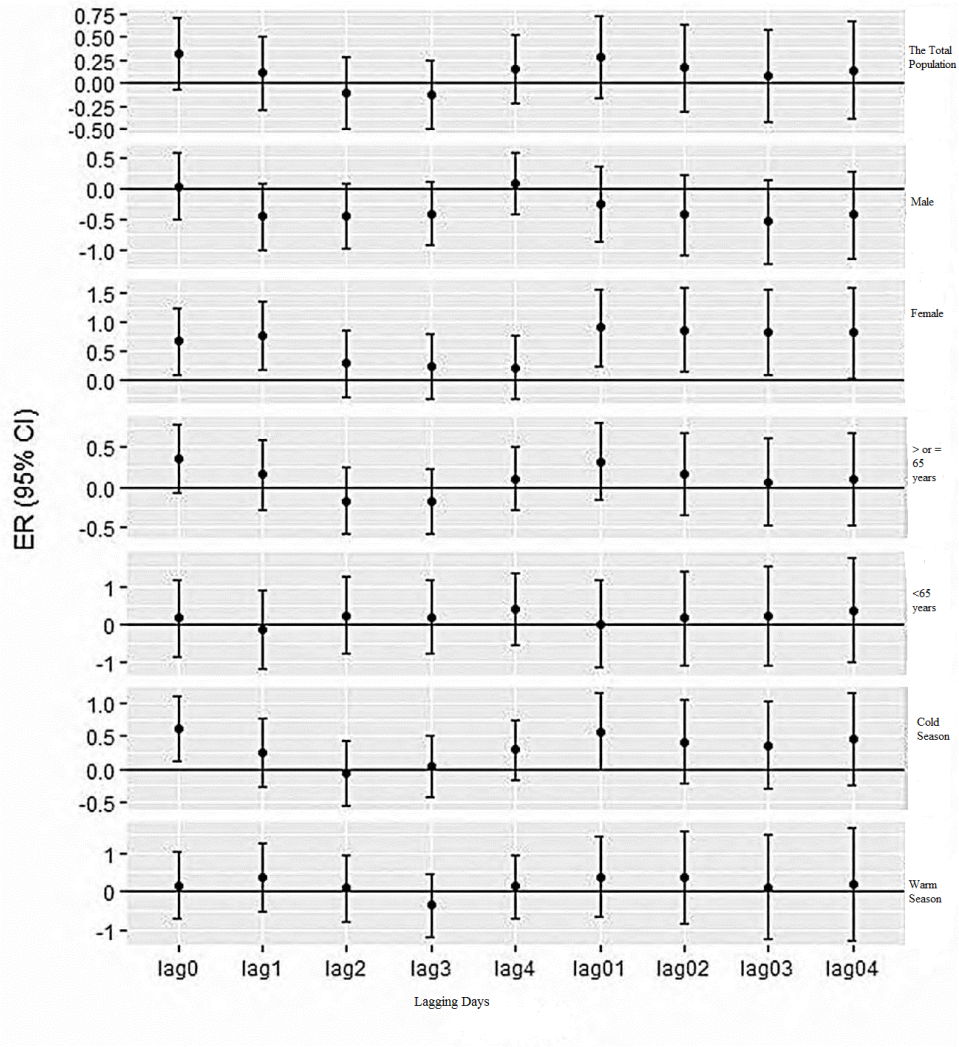

Figure 1. Effects of NO_2 concentration changes on daily death from cardiovascular and cerebrovascular diseases in Enshi City from 2015 to 2018.

3.2.2. Double pollutant model results

The double pollutant model results (**Figure 2**) show that after introducing other gaseous pollutants (SO_2, Co, O_3) into the NO_2 single pollutant model, the impact of NO_2 on the death risk of cardiovascular and cerebrovascular diseases in women and cold season subgroups still exists, but the estimated value of the effect will change slightly. Among them, the introduction of CO into the model of female subgroup has the greatest impact on the results. The risk of death from cardiovascular and cerebrovascular diseases in the female population of lag01 will increase to 0.97% (0.30%~1.65%) ($P < 0.05$); Adding SO_2 to the model of the cold season subgroup has the greatest impact on the results. The risk of death from cardiovascular and cerebrovascular diseases in the whole population of lag0 will be reduced to 0.40% (0.13%~0.94%), and the result difference is not statistically significant.

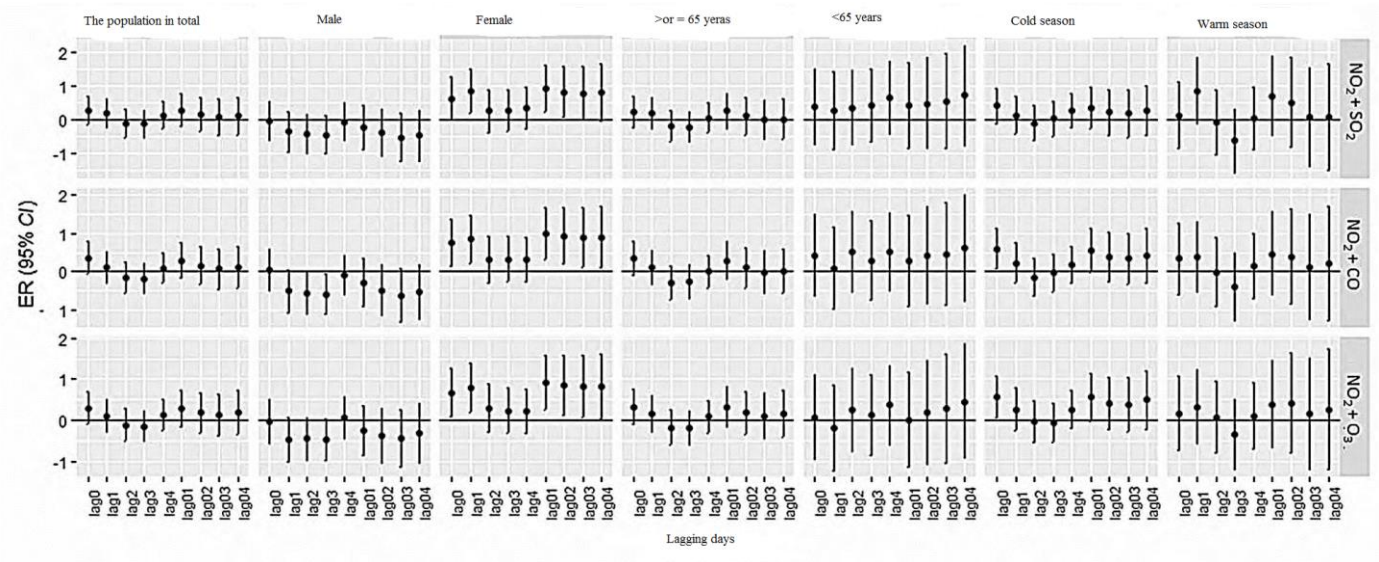

Figure 2. Results of two pollutant models for general population and subgroups.

3.2.3. Sensitivity analysis

The purpose of sensitivity analysis is to evaluate the stability of the results by changing the degree of freedom of time trend (*df* = 68) and meteorological elements (*df* = 35). The results of sensitivity analysis suggest that the model fits well and the results are robust.

4. Discussion

The study found that the increase of atmospheric NO_2 in Enshi City with low pollution level will not significantly increase the death risk of cardiovascular disease in the general population; however, for female population and the whole population in cold season, even at low pollution level, the death risk of cardiovascular disease will increase significantly with the increase of NO_2 concentration.

Under the background of different concentrations of air pollutants, the impact law of air pollutants on population health may be different [7,8]. Consistent with the results of a study carried out by Qin Meng and others in Fengxian District, Jiangxi Province, which is close to the concentration level of NO_2 in Enshi City [16], it is also not observed that the increase of atmospheric NO has a significant impact on the increase of death risk of cardiovascular disease in the general population. However, a study in Beijing found that for every quartile increase in NO_2 concentration, the death risk of cardiovascular and cerebrovascular diseases in the total population of the city will increase by 4.11% [17]. During the study period, the average concentration of no in the city was 55.00 $\mu g/m^3$, significantly higher than that of Enshi City. The above results suggest that the effects of high pollution level and low pollution level atmospheric NO_2 on people's health may be different. However, it is unclear whether this conclusion is applicable to specific populations or specific seasonal conditions to solve this problem, subgroup analysis was carried out.

The results of gender subgroup show that NO_2 exposure has a significant impact on the increased risk of death from cardiovascular and cerebrovascular diseases in female residents of Enshi City, but no significant effect is found in male subgroup

Studies in Ho Chi Minh City, Vietnam [18] and Wuhan City, Hubei [19] also found that NO_2 has a greater impact on the health of women's cardiovascular and cerebrovascular diseases than men NO_2 exposure will have harmful effects on cardiovascular and cerebrovascular systems, including oxidative stress, atherosclerosis and abnormal lipid metabolism [20]. When Guo et al. studied the oxidative stress and chromosome damage caused by PAH exposure, they found that women are more vulnerable to oxidative stress [21], which may be one of the reasons why women are more sensitive than men.

The results of seasonal subgroups showed that NO_2 exposure in cold season had a significant impact on the increased risk of death from cardiovascular and cerebrovascular diseases in the whole population of Enshi City, while no significant effect was found in warm season subgroups. A time series analysis in Beijing [22] also found that the harmful effect of pollutants is more obvious in cold seasons when studying the impact of air pollutants on the admission rate of cardiovascular and cerebrovascular diseases. The effect of NO_2 on the death risk of cardiovascular and cerebrovascular diseases in cold season is more significant than that in warm season, which may be related to the vascular injury caused by low temperature. Cold exposure can cause vasoconstriction to reduce skin blood flow and prevent heat loss, but long-term contraction can lead to ischemia and potential irreversible damage [23].

In conclusion, in areas with low atmospheric NO_2 pollution level, the increase of its concentration will increase the risk of death from cardiovascular and cerebrovascular diseases among women and the whole population in cold season, and the impact still exists after controlling the effects of other gaseous pollutants. Therefore, even in low pollution areas, attention should be paid to the prevention and control of health hazards of air pollution. It is suggested to consider the impact of seasonal factors on human health, take different measures in different seasons, and pay attention to the health protection of key groups such as women.

Conflict of interest: The authors declare no conflict of interest.

References

1. Xu R, Zhang H, Pan J, et al. Research Progress on the effects of short-term exposure to air pollutants on cardiac arrest events. Public health and preventive medicine. 2020; 31(3): 112-116.
2. Eum KD, Kazemiparkouhi F, Wang B, et al. Long-term NO2 exposures and cause-specific mortality in American older adults. Environment International. 2019; 124: 10-15. doi: 10.1016/j.envint.2018.12.060
3. Li Y, Xu R, Zhang H, et al. Effects of atmospheric fine particulate matter exposure on ischemic heart disease. Public health and preventive medicine. 2021; 32(4): 120-125.
4. Huang L, Li J, Liu F, et al. Time series study on the impact of air pollutants on the death of permanent residents in Yancheng City. Public health and preventive medicine. 2021; 32(4): 18-22.
5. Tan F, Wang W, Qi S, et al. Air pollutants and outpatient visits for cardiovascular disease in a severe haze-fog city: Shijiazhuang, China. BMC Public Health. 2019; 19(1). doi: 10.1186/s12889-019-7690-4
6. Liu Y, Sun J, Gou Y, et al. Analysis of Short-Term Effects of Air Pollution on Cardiovascular Disease Using Bayesian Spatio-Temporal Models. International Journal of Environmental Research and Public Health. 2020; 17(3): 879. doi: 10.3390/ijerph17030879
7. Taj T, Stroh E, Åström DO, et al. Short-Term Fluctuations in Air Pollution and Asthma in Scania, Sweden. Is the Association Modified by Long-Term Concentrations? Larcombe A, ed. PLOS ONE. 2016; 11(11): e0166614. doi: 10.1371/journal.pone.0166614

8. Shan J, Li HY, Liu GF, et al. Effect of air pollution on health service demand of the elderly and middle-age patients with hypertension, cardiovascular and cerebrovascular diseases: based on analysis of data from CHARLS. Health sciences. 2016; 48(3): 460-464.
9. Health statistics and information center of the Ministry of health Application instruction manual of international classification of diseases (ICD 10). Beijing: Peking Union Medical University Press; 2001.
10. Cao X, Cui X, Wang B, et al. Cause of death monitoring and life loss analysis of permanent residents in Enshi City from 2013 to 2018. Public health and preventive medicine. 2021; 32(1): 27-31.
11. Wang F, Liu H, Li H, et al. Ambient concentrations of particulate matter and hospitalization for depression in 26 Chinese cities: A case-crossover study. Environment International. 2018; 114: 115-122. doi: 10.1016/j.envint.2018.02.012
12. Wang L, Liu C, Meng X, et al. Associations between short-term exposure to ambient sulfur dioxide and increased cause-specific mortality in 272 Chinese cities. Environment International. 2018; 117: 33-39. doi: 10.1016/j.envint.2018.04.019
13. Yin P, Chen R, Wang L, et al. Ambient Ozone Pollution and Daily Mortality: A Nationwide Study in 272 Chinese Cities. Environmental Health Perspectives. 2017; 125(11). doi: 10.1289/ehp1849
14. Song G, Zhu L, Gao A, et al. Blockwise AICc and its consistency properties in model selection. Communications in Statistics - Theory and Methods. 2019; 50(13): 3198-3213. doi: 10.1080/03610926.2019.1691734
15. Liu C, Liu Y, Zhou Y, et al. Short-term effect of relatively low level air pollution on outpatient visit in Shennongjia, China. Environmental Pollution. 2019; 245: 419-426. doi: 10.1016/j.envpol.2018.10.120
16. Qin M, Li J, Chen L, et al. Study on the impact of major air pollutants on the death of local residents from circulatory system diseases in Fengxian District. Journal of Southeast University (Medical Edition). 2014; 33(3): 304-310.
17. Li W, Cao Y, Li R, et al. The spatial variation in the effects of air pollution on cardiovascular mortality in Beijing, China. Journal of Exposure Science & Environmental Epidemiology. 2018; 28(3): 297-304. doi: 10.1038/jes.2016.21
18. Phung D, Hien TT, Linh HN, et al. Air pollution and risk of respiratory and cardiovascular hospitalizations in the most populous city in Vietnam. Science of The Total Environment. 2016; 322-330. doi: 10.1016/j.scitotenv.2016.03.070
19. Zhong P, Huang S, Zhang X, et al. Individual-level modifiers of the acute effects of air pollution on mortality in Wuhan, China. Global Health Research and Policy. 2018; 3(1). doi: 10.1186/s41256-018-0080-0
20. Stieb DM, Berjawi R, Emode M, et al. Systematic review and meta-analysis of cohort studies of long term outdoor nitrogen dioxide exposure and mortality. Forloni G, ed. PLOS ONE. 2021; 16(2): e0246451. doi: 10.1371/journal.pone.0246451
21. Guo H, Huang K, Zhang X, et al. Women are more susceptible than men to oxidative stress and chromosome damage caused by polycyclic aromatic hydrocarbons exposure. Environmental and Molecular Mutagenesis. 2014; 55(6): 472-481. doi: 10.1002/em.21866
22. Amsalu E, Wang T, Li H, et al. Acute effects of fine particulate matter (PM2.5) on hospital admissions for cardiovascular disease in Beijing, China: a time-series study. Environmental Health. 2019; 18(1). doi: 10.1186/s12940-019-0506-2
23. Pan Y, Thapa D, Baldissera L, et al. Relevance of TRPA1 and TRPM8 channels as vascular sensors of cold in the cutaneous microvasculature. Pflügers Archiv - European Journal of Physiology. 2017; 470(5): 779-786. doi: 10.1007/s00424-017-2085-9