Short-Term Effects of Ambient Air Pollution On Daily Emergency Room Visits for Abdominal Pain: A Time-Series Study in Wuhan, China

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Abstract

Background

There are few studies focused on the correlations between ambient air pollution and abdominal pain, especially in emergency departments in China.

Method:

Daily data (from January 1, 2016 to December 31, 2018), including air pollution concentration (SO\textsubscript{2}, NO\textsubscript{2}, PM\textsubscript{2.5}, PM\textsubscript{10}, CO, and O\textsubscript{3}) and meteorological variables, for daily emergency room visits (ERVs) were collected in Wuhan, China. We conducted a time-series study to investigate the potential correlation between six ambient air pollutants and ERVs for abdominal pain and their effects, in different genders, ages and seasons.

Results

A total of 16,306 abdominal pain ERVs were identified during the study period. A 10-µg/m\textsuperscript{3} increase in concentration of SO\textsubscript{2}, NO\textsubscript{2}, PM\textsubscript{2.5}, PM\textsubscript{10}, CO, and O\textsubscript{3} corresponded respectively to incremental increases in abdominal pain of 6.12% (95% confidence interval [CI]: -0.44-13.12), 1.65% (95%CI: -0.25-3.59), 1.12% (95%CI: -0.18-2.44), 0.38% (95%CI: -1.09-1.87), 9.87% (95%CI:3.14–17.05) and 1.11% (95%CI: 0.03–2.21). We observed significant correlations between CO and O\textsubscript{3} and daily abdominal pain ERVs increase, and positive but insignificant correlations between the other pollutants and ERVs. The effects were stronger mainly for females (especially SO\textsubscript{2} and O\textsubscript{3}) and younger people (especially CO and O\textsubscript{3}). The correlations of PM\textsubscript{2.5} and PM\textsubscript{10} were stronger in cool seasons, while the correlation of CO was stronger in warm seasons.

Conclusion

Our time-series study suggested that short-term exposure to air pollution (especially CO and O\textsubscript{3}) was positively correlated with ERVs for abdominal pain in Wuhan, China, and that their effects varied by season, gender and age. These data can add evidence on how air pollutants affect the human body, and may prompt hospitals to take specific precautions on polluted days and maintain order in emergency departments made busier due to the pollution.

Introduction

The Global Burden of Disease study identified air pollution as a leading cause of global disease burden, especially in developing countries.(Collaborators 2018) Short-term exposure to ambient air pollution can acutely deteriorate respiratory, cardiovascular and digestive diseases, leading to increased emergency room visits (ERVs).(Rodopoulou, Samoli et al. 2015, Al Ahad, Sullivan et al. 2020, Vignal, Guilloteau et al. 2021) Since Wuhan is one of the twenty most polluted cities with a large number of daily ERVs in China, which is the biggest developing country in the world, it is important to figure out potential health risks from ambient air pollution.

Recently, there has been an accumulation of articles revealing the effects of air pollution on emergency departments, (Rodopoulou, Samoli et al. 2015, Chen, Zheng et al. 2019) which plays a significant role in dealing with public health events, meeting the needs of patients and improving the treatment success rate. However, overcrowding of emergency
departments is an international issue, among which abdominal pain is the most significant proportion. (Hooker, Mallow et al. 2019) The most common diseases manifesting abdominal pain in ERVs are gastroenteritis, cholecystitis, and urolithiasis which will cause acute and serve pain thus need emergency treatments. Environmental pollution has been noted to play an important role in the development of these diseases. For instance, exposure to the particulate matter may lead to urolithiasis increase, by causing urine volume decreases through vascular endothelial injury, systemic inflammation, atherosclerosis and microvascular changes. (Sun, Wang et al. 2005, Chow, Watson et al. 2006) Air pollution exposure can increase the hospitalizations for digestive diseases, including inflammatory bowel disease, peptic ulcers, and enteritis. (Ananthakrishnan, McGinley et al. 2011, Xu, Kan et al. 2016, Tsai, Chiu et al. 2019, Gu, Shi et al. 2020) although the mechanisms remain unclear and inconclusive. However, studies focus the pollution effects on specific diseases or symptoms in ERVs, such as abdominal, are still lacking. It will be favorable for hospitals to figure out the correlations between air pollution and abdominal pain, and thereby to understand the characteristics of ERVs, take precautions and maintain order in specific and heavy polluted days.

Considering the above-mentioned, we conducted this time-series study to analyze the correlations between six ambient air pollutants (SO$_2$, NO$_2$, PM$_{2.5}$, PM$_{10}$, CO, O$_3$) and ERVs for abdominal pain, in Zhongnan Hospital of Wuhan University from 1 January 2016 to 31 December 2018. We also analyzed the discrepancy correlation between different seasons, gender and age. In addition, we explored the exposure-response relationship curves between ERVs for abdominal pain and air pollutants, as well as the co-effects among six air pollutants. It should be useful in risk assessment, resources allocation and health policy making.

**Materials And Methods**

Wuhan is the capital of Hubei Province, with a population size over 10 million, and lying in Central China (latitude 30°35'N and longitude 114°17'E), and covering 8494.41km$^2$. It consists of seven central districts, and six suburban and rural districts (Fig. 1). Because it is an essential industrial and transport interchange of China, the main causes of air pollution are vehicle exhaust, coal-fired heating, and industrial emissions. (Ren, Li et al. 2017) Wuhan has a humid monsoon subtropical climate. Summers are hot and wet while winters are cold and dry. The average temperature is 29°C in July and 4°C in January.

**Emergency room visits data**

We were provided with the daily number of ERVs from January 1, 2016 to December 31, 2018, from Zhongnan Hospital of Wuhan University in Wuhan, China. A doctor's team discussed the disease diagnoses, corrected them to standard names, and re-matched them to an accurate International Classification of Disease Code, revision 10 (ICD-10). From the ERV records, we specifically selected those outpatient visits whose chief complaint was abdominal pain. The research protocol was approved by the Medical Ethics Committee of Zhongnan Hospital. (IRB number: 2021018K)

**Environmental and meteorological data**

We acquired daily ambient air pollution data (SO$_2$, NO$_2$, PM$_{2.5}$, PM$_{10}$, CO, and O$_3$) from January 2016 to December 2018, from the website of the Wuhan Ecological Environment Bureau (http://hbj.wuhan.gov.cn/). The daily average concentrations of air pollutant were calculated by average hourly values from ten fixed-site stationary centers, which can cover the urban districts of Wuhan. All the stations are located away from industrial, residential, and vehicle sources, to make sure they can monitor the representative measurements of background pollution, without undue interference.
The data of two meteorological parameters during the study period (average daily temperature [°C] and relative humidity [%]) were acquired from the Meteorological Data Sharing Service System of China Meteorological Administration (Beijing, China). Dates with missing data were eliminated from our study.

**Statistical analysis**

We chose the over-dispersed generalized additive model (GAM) to perform a time-series analysis to explore the acute effect of air pollutants on ERVs with abdominal pain, in order to control for both time-invariant and time-varying confounders. Some covariates were added into the main model. First, a natural cubic regression smoothing function of calendar time with 7 degrees of freedom (df) per year excluded unmeasured long-term and seasonal trends longer than two months. (Chen, Lin et al. 2018) Second, a natural smooth function of the average daily temperature (6 df) and relative humidity (3 df) controlled for the nonlinear confounding effects of weather conditions. (Zhou, Geng et al. 2021) Third, other covariates such as day of the week (DOW) and public holidays (Holiday) were controlled as dummy variables in the basic models.

The core model can be described as follows:

\[
\log(E(Y_t)) = \beta Z_t + DOW + \text{ns}(\text{time}, \text{df}) + \text{ns}(\text{temperature}, 6) + \text{ns}(\text{humidity}, 3) + \text{intercept}
\]

where \(E(Y_t)\) represents the number of abdominal pain count for day \(t\); \(\beta\) represents the log-related rate of EVRs with abdominal pain associated with a unit increase of air pollutants; \(Z_t\) refers to the pollutant concentrations at day \(t\); DOW is a dummy variable for day of the week; and ns() means the natural cubic regression smooth function. We plotted the exposure-response relationship curves between air pollutant and ERVs with abdominal pain by adding to the above model a spline function with 3 df.

We conducted 4 sensitivity analyses to ensure the stability of our models. First, Two-pollutant models can examine the robustness of effect estimates. Co-pollutants with a correlation coefficient < 0.7 would be added to the model. Second, we conducted two different lag constructions: single-day lags (lag0 to lag7), and moving average lags (lag 01 to lag 07). Third, we selected alternative df with 4~10 per year. Besides, since air pollution levels vary by season, (Wang, Wang et al. 2018) we divided our analyses into the cool period (October to March) and the warm period (April to September), and reduced the df per year from 7 year-round to 4 in the cool-period and warm-period analyses.

All statistical models were run in R software (version 3.6.0) using the MGCV package. The statistical tests were two-sided, with correlations with \(p < 0.05\) mean statistically significant. The effects are described as the percent changes and 95% CI in daily ERVs for abdominal pain per 10 µg/m\(^3\) increase of each pollutant.

**Result**

We obtained data from 152,830 ERVs in Zhongnan Hospital (from January 1, 2016 to December 31, 2018), among which 16,306 were caused by abdominal pain. Females and younger people (< 45 years old) constituted respectively 52.5% and 58.2% of the visits. Total ERVs for abdominal pain were slightly higher in the warm seasons than in the cool seasons (8331 vs. 7975). The means of daily temperature and relative humidity were 17.87 °C and 74.99%, respectively. (Table 1) Daily average concentrations were 9.42 µg/m\(^3\) for SO\(_2\), 58.89 µg/m\(^3\) for NO\(_2\), 68.71 µg/m\(^3\) for PM\(_{2.5}\), 64.8 µg/m\(^3\) for PM\(_{10}\), 25.06 µg/m\(^3\) for CO and 48.4 µg/m\(^3\) for O\(_3\). During our study period, there were 382 (24.8%) and 229 (20.9%) days respectively where PM\(_{2.5}\) and NO\(_2\) exceeded Chinese secondary ambient air quality standards. Other pollutants were within this standard range most of the time.
Table 1
The summary of daily air pollutants, weather conditions, and daily emergency room visit for abdominal pain (N = 16,306) during our study period (January 1, 2016 to December 31, 2018)

| Air pollutant concentration (µg/m3) a | Mean | SD | Min | P25 | Median | P75 | Max |
|--------------------------------------|------|----|-----|-----|--------|-----|-----|
| SO₂                                 | 9.42 | 5.33 | 2.7 | 5.5 | 7.9 | 12.03 | 35.67 |
| NO₂                                 | 58.89 | 22.68 | 17.5 | 40.4 | 56.16 | 75.92 | 122.5 |
| PM₂.₅                               | 68.71 | 39.47 | 9.9 | 41.08 | 60.63 | 86.53 | 254.7 |
| PM₁₀                                | 64.8 | 28.17 | 8.6 | 48.3 | 63 | 79 | 461.5 |
| CO                                  | 25.06 | 7.49 | 8.9 | 19.8 | 23.8 | 29.3 | 59.3 |
| O₃                                  | 48.4 | 31.52 | 2.1 | 24.8 | 39.8 | 67.3 | 190 |

**Meteorological measures**

| Temperature (°C) | Mean | SD | Min | P25 | Median | P75 | Max |
|------------------|------|----|-----|-----|--------|-----|-----|
| Humidity (%)     | 74.99 | 13.38 | 36 | 65.25 | 75.75 | 85.5 | 100 |

**No. of emergency room visit for abdominal pain**

| Season(N) | 15 | 8 | 1 | 9 | 13 | 20 | 42 |
|------------|----|----|---|---|----|----|----|
| Warm b     | 15 | 8 | 1 | 9 | 13 | 20 | 42 |
| Cool c     | 15 | 7 | 1 | 8 | 13 | 20 | 37 |

**Gender(N)**

| Male | 7 | 4 | 0 | 4 | 6 | 10 | 25 |
|------|---|---|---|---|---|----|----|
| Female | 8 | 4 | 0 | 5 | 7 | 11 | 25 |

**Age(N)**

| < 45 | 9 | 5 | 0 | 5 | 8 | 12 | 31 |

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a 24-hour average for PM₂.₅, PM₁₀, SO₂, and NO₂; maximal 8-h average for O₃

b Warm season: from April to September.

C Cool season: from October to March.

Abbreviations: SD, standard deviation; P25, 25th percentile; P75, 75th percentile;

PM₂.₅, particulate matter with an aerodynamic diameter less than or equal to 2.5 µm;

PM₁₀, particulate matter with an aerodynamic diameter less than or equal to 10 µm;

O₃, ozone; SO₂, sulfur dioxide; NO₂, nitrogen dioxide; CO, carbon monoxide.
|       | Mean | SD | Min | P25 | Median | P75 | Max |
|-------|------|----|-----|-----|--------|-----|-----|
| ≥ 45 | 6    | 4  | 0   | 3   | 6      | 8   | 24  |

\(^a\)24-hour average for PM\(_{2.5}\), PM\(_{10}\), SO\(_2\), and NO\(_2\); maximal 8-h average for O\(_3\).

\(^b\) Warm season: from April to September.

\(^c\) Cool season: from October to March.

Abbreviations: SD, standard deviation; P25, 25th percentile; P75, 75th percentile;

PM\(_{2.5}\), particulate matter with an aerodynamic diameter less than or equal to 2.5 µm;

PM\(_{10}\), particulate matter with an aerodynamic diameter less than or equal to 10 µm;

O\(_3\), ozone; SO\(_2\), sulfur dioxide; NO\(_2\), nitrogen dioxide; CO, carbon monoxide.

Generally, there were moderate to strong positive correlations between the six pollutants (Spearman's correlation coefficient ranged from 0.55 to 0.87, Fig. 2) except for O\(_3\), which showed weak correlations with other pollutants (-0.26-0.09). Humidity and temperature were mostly negatively correlated with these pollutants (-0.46-0.01).

Figure 3 presents the percent change in abdominal pain ERVs per 10 µg/m\(^3\) increase of pollutants concentration, while using different single day lag (lag1-lag7) and multiple-day lags (lag01-lag07). Overall, we found statistically significant relationships between CO, O\(_3\) and abdominal pain ERVs, while other pollutants showed positive but insignificant correlations. Lag01 for SO\(_2\) and O\(_3\), lag06 for NO\(_2\), PM\(_{10}\) and CO, and lag07 for PM\(_{2.5}\) produced the largest estimates. 10µg/m\(^3\) increases of SO\(_2\), NO\(_2\), PM\(_{2.5}\), PM\(_{10}\), and O\(_3\) were correlated respectively with incremental increases in daily ERVs for abdominal pain of 6.12% (95% CI: -0.44–13.12), 1.65% (95% CI: -0.25–3.59), 1.12% (95% CI: -0.18–2.44), 0.38% (95% CI: -1.09–1.87), 9.87% (95% CI: 3.14–17.05) and 1.11% (95% CI: 0.03–2.21). (Table S1)

The exposure-response (E-R) curves for the correlations between pollutants at their peak lag day and abdominal pain ERVs were generally positive (Fig. 4). The E-R curve of SO\(_2\) showed a slowly growing slope. The E-R curves of NO\(_2\) and CO increased sharply before the concentrations ≥ 50 µg/m\(^3\) and ≥ 20 µg/m\(^3\) respectively, and then showed just a slight rise. The E-R curve of PM\(_{2.5}\) was nearly J-shaped, increasing sharply at the concentrations ≤ 50 µg/m\(^3\) and ≥ 100 µg/m\(^3\). The E-R curves of PM\(_{10}\) and O\(_3\) were rising slopes at concentrations ≤ 60 µg/m\(^3\) and ≤ 100 µg/m\(^3\) respectively, then became flat.

Table 2 summarizes the results for possible effects modified by season, gender and age. It shows that PM\(_{2.5}\) and PM\(_{10}\) were significantly related to abdominal pain ERVs in cool seasons while CO was significantly related in warm seasons. A 10 µg/m\(^3\) increase of PM\(_{2.5}\) and PM\(_{10}\) in cool seasons corresponded respectively to 1.70% (95% CI: 0.16–3.26) and 2.41% (95% CI: 0.21–4.66) increases in ERVs, while in warm seasons, it related to 1.20% and 0.63% increases, respectively (P < 0.05). By contrast, a 10 µg/m\(^3\) increase of CO in warm seasons corresponded to a 20.82% incremental increase of ERVs (95% CI: 6.59–36.95), compared to 5.63% increments in cool seasons (P < 0.05). The influence of SO\(_2\) and O\(_3\) were more obvious on females than on males (13.65% vs. -2.34%; 1.54% vs. 0.56%, respectively, P < 0.05). For CO and O\(_3\), the correlations were stronger among younger people (< 45 years old) than elders (10.47% vs. 0.31%; 1.65% vs. 0.27%, respectively, P < 0.05).
Table 2
Percent change (95% CI) in abdominal pain ERVs with a 10 µg/m3 increase in air pollutant concentrations by season, gender and age in Wuhan, China.

| Pollutants | Season | Gender | Age |
|------------|--------|--------|-----|
|            | Cool   | Warm   | Male | Female | Younger | Elder |
| SO₂ a      | 0.71 (-0.44,1.88) | 8.49 (-5.65,24.74) | -2.34 (-10.76,6.88) | 13.65 (4.56,23.53) | 4.71 (-3.94,14.14) | 7.16 (-2.08,17.28) |
| NO₂ b      | -0.01 (-2.62,2.67) | 1.25 (-2.25,4.88) | 1.97 (-0.59,4.59) | 1.29 (-1.07,3.70) | 2.18 (-0.25,4.68) | 0.95 (1.60,3.57) |
| PM₂.₅ c    | 1.70 (0.16,3.26) * | 1.20 (-2.15,4.66) | 1.54 (-0.21,3.32) | 1.06 (-0.55,2.69) | 1.52 (-0.15,3.23) | 0.97 (-0.76,2.73) |
| PM₁₀ b     | 2.41 (0.21,4.66) * | 0.63 (-1.86,3.18) | 0.98 (-0.99,2.99) | 1.35 (-0.44,3.18) | 1.40 (-0.46,3.29) | 0.98 (-0.99,2.99) |
| CO b       | 5.63 (-2.22,14.12) | 20.82 (6.59,36.95) * | 4.85 (-3.75,14.21) | 7.06 (-1.06,15.85) | 10.47 (1.85,19.83) | 0.31 (-7.92,9.27) |
| O₃ a       | 1.13 (-1.45,3.77) | 1.13 (-1.45,3.77) | 0.56 (-0.92,2.06) | 1.54 (0.16,2.93) * | 1.65 (0.26,3.05) * | 0.27 (-1.25,1.82) |

* p < 0.05.

a Moving average of lag 01 was used for SO₂, and O₃.

b Moving average of lag 06 were used for NO₂, PM₁₀ and CO.

c Moving average of lag 07 was used for PM₂.₅.

Pollutants with < 0.7 Spearman correlation co-efficient were added into two-pollutant models, and most models remained stable after adjusting for co-pollutants. Especially for CO, its positive relation with daily ERVs for abdominal pain remained significantly robust after adjustment (Table 3). Another sensitivity analysis proved that alternative df (4–10) did not significantly affect the effects of pollutants on abdominal pain ERVs (Figure S1).
Table 3
Percent change (%, mean and 95% CI) in ERVs for abdominal pain in two-pollutant models.

| Two-pollutants | Estimate          |
|----------------|-------------------|
| SO₂            | -                 |
|                | 6.12 (-0.44,13.12)|
| +PM₂.5         | 5.67 (-1.55,13.43)|
| +CO            | 4.92 (-2.52,12.93)|
| +O₃            | 4.66 (-2.22,12.02)|
| NO₂            | -                 |
|                | 1.65 (-0.25,3.59) |
| +PM₂.5         | 1.13 (-1.12,3.43) |
| +CO            | 0.39 (-1.71,2.53) |
| +O₃            | 1.32 (-0.80,3.49) |
| PM₂.5          | -                 |
|                | 1.12 (-0.18,2.44) |
| +SO₂           | 1.00 (-0.50,2.52) |
| +NO₂           | 0.85 (-0.70,2.43) |
| +O₃            | 0.96 (-0.45,2.39) |
| PM₁₀           | -                 |
|                | 0.38 (-1.09,1.87) |
| +O₃            | -0.24 (-1.87,1.41)|
| CO             | -                 |
|                | 9.87 (3.14,17.05) *|
| +SO₂           | 10.10 (3.01,17.68) *|
| +NO₂           | 9.47 (2.00,17.48) *|
| +PM₁₀          | 12.40 (4.67,20.70) *|
| +O₃            | 9.58 (2.71,16.92) *|
| O₃             | -                 |
|                | 1.11 (0.03,2.21) *|
| +SO₂           | 0.95 (-0.17,2.08) |
| +NO₂           | 0.97 (-0.16,2.12) |

* p < 0.05.

Moving average of lag 01 was used for SO₂ and O₃.
Moving average of lag 06 were used for NO₂, PM₁₀ and CO.
Moving average of lag 07 was used for PM₂.5.
Discussion

Abdominal pain is one of the most common reasons for ERVs (Hooker, Mallow et al. 2019), and few studies have explored the acute effect of ambient air pollution on abdominal pain, especially in emergency room visits. Overall, our study suggests that short-term exposure to air pollutants, including CO and O₃, is significantly correlated with increased risks of abdominal pain ERVs. The correlations between CO and abdominal pain ERVs was robust after adjustment in two-pollutant models. The correlations were stronger mainly on females (especially SO₂ and O₃) and younger people (especially CO and O₃). The correlations of PM₂.₅ and PM₁₀ were stronger in cool seasons, but for CO stronger in warm seasons. Our findings have added evidence on how air pollutants affect the human body, and may help hospitals take precaution in polluted days and maintain order in emergency departments made busier due to the pollution.

During our study period, the mean concentrations of PM₂.₅ (68.71 µg/m³) and NO₂ (58.89 µg/m³) in Wuhan exceeded the Chinese National Ambient Air Quality Standards (35 and 40 µg/m³). Urban expansion, industrial development, the increase of motor vehicles, and an aging population are major contributors to the effects of severe pollution. However, it is promising that the overall trend of air quality is improving. (Huang, Pan et al. 2018)

Our study proved that short-term exposure of ambient air pollutants (SO₂, NO₂, PM₁₀, PM₂.₅, CO, O₃) have positive correlations with the ERVs for abdominal pain, especially CO and O₃. Highly elevated or protracted CO exposures may produce untoward biological oxidations, and interfere with homeostasis. (Plantadosi 2008) CO can readily absorbed from the lungs into the bloodstream, forms carboxyhemoglobin with hemoglobin, thus resulting in tissue hypoxia. And the relationships between lipid peroxidation and membrane fatty acid composition in CO intoxication may be a potential mechanism. (Akyol, Erdogan et al. 2014) The cooperation of CO and PM₂.₅ may also enhance the damage which was also showed in our study (the Spearman correlation co-efficient of them > 0.7) but this is still not certain. (Chen, Gokhale et al. 2007) For O₃, the toxicity was due mainly to its action as an oxidant, causing lipid peroxide decomposition, and inflammatory and blood rheology. (Mehlman and Borek 1987, Yang, Li et al. 2019) The systemic response may also affect the digestive and urinary systems, and lead to abdominal pain. Although O₃ has been regarded as a kind of medical drug gradually, we still suggest more attention to its effect of different concentrations and the particular biological system where it acts. (Zanardi, Borrelli et al. 2016)

The positive results varied also by season, sex, and age. In our study, CO demonstrated a stronger effect in warm seasons than in cool seasons. This may be because of the extremely hot weather from July to September in Wuhan,
leading to more fluid loss cooperating with CO and increasing the risk of hypoxia. Vasoconstrictions happen in the digestive and urinary systems, and can result in abdominal pain. Many studies showing ambient pollutants having more serious effect on elders are contrary to our results, which showed that CO and O$_3$ affected younger people more. (Bell, Zanobetti et al. 2013) Since our study data were from emergency departments, most of the visits with abdominal pain were acute and inflammatory. Younger people usually have more outdoor activities, and thus more chance to ingest pollutants than elders do. Another possible explanation is that the effects on elders center mainly on the cardiovascular system rather than the digestive or urinary systems. We found also that females were more likely to suffer the effects of SO$_2$ and O$_3$ increases. This phenomenon was proved in the respiratory and cardiovascular systems as well. (Tseng, Huang et al. 2012, Birukova, Cyphert-Daly et al. 2019) In our study, PM$_{2.5}$ and PM$_{10}$ demonstrated higher effects during cool seasons, which was consistent with previous studies. (Zhang and Cao 2015, Song, Lu et al. 2018) Their studies attributed the correlations to the increase in coal burning in households as the source of heat, and to the unfavorable meteorological conditions in winter, which limit the dispersion of air pollutants. (Zhang and Cao 2015)

However, excessive focus on the effects of a single pollutant may ignore the cooperation between pollutants. Population-based observational studies should consider the correlations between them. (Chen, Gokhale et al. 2007) The exposure-response observational curves are crucial tools for public health assessment. We did not observe evident threshold concentrations above which NO$_2$, PM$_{2.5}$ and CO were not correlated with ERVs. Interestingly, we observed a J-shaped relationship between PM$_{2.5}$ and abdominal pain ERVs, which need in future studies to be considered when investigating health effects of PM$_{2.5}$.

The most common acute diseases in ERVs for abdominal pain are gastroenteritis, cholecystitis, and urolithiasis. The correlations between gastrointestinal diseases and air pollution have been widely discussed in recent years. Studies showed that air pollution exposure may increase the risk of appendicitis, as well as hospitalizations for inflammatory bowel disease, peptic ulcers, and enteritis. (Kaplan, Dixon et al. 2009, Ananthakrishnan, McGinley et al. 2011, Xu, Kan et al. 2016, Tsai, Chiu et al. 2019) A study in Canada found that air pollution may cause non-specific abdominal pain, especially in young ladies, which is consistent with our studies. (Kaplan, Szyszkowicz et al. 2012) The main mechanisms for pollutants increasing gastrointestinal diseases include directly toxic effects, systemic inflammation, immune activation, gut microbiota effects, and gut permeability effects (Beamish, Osornio-Vargas et al. 2011, Mutlu, Engen et al. 2011).

Cholecystitis caused by gallstone is one of the most common diseases in emergency department visits. There have been not studies investigating the correlation between ambient air pollution and cholecystitis at present. Actually, cholecystic diseases have a close relationship with liver diseases but more common than them in emergency department. Studies have revealed that the obstruction of cholecystitis may result in hepatic inflammatory changes and make liver diseases progress to secondary biliary cirrhosis. (Flinn, Olson et al. 1977, Geraghty and Goldin 1994) And chronic liver diseases will impair the gallbladder contractility and contribute to the increased gallstone formation in return. (Acalovschi, Dumitrascu et al. 2004) Long-term exposure to environmental pollutants may lead to liver abnormality or injury by activating reactive oxygen species (ROS) production and initial immune response (Sanchez-Valle, Chavez-Tapia et al. 2012, Kim, Park et al. 2014) which were all chronic effect on liver. As for acute effect, we suppose maybe ambient air pollution also has positive correlation with cholecystitis through causing dyslipidemia (Zhang, Wang et al. 2021) which was considered as a risk factor of gallstones and cholecystitis. (Lammert, Gurusamy et al. 2016) Whether the liver injuries or the cholecystic diseases are the initiating agents for acute hepatobiliary diseases is still uncertain.
Furthermore, air pollution may increase the risk of bladder, kidney and urinary tract cancer, as well as other more benign diseases.\cite{Al-Aly2020,ZareSakhvidi2020} In an emergency department, the most common visits for abdominal pain in urinary system are for urolithiasis. The effects of particulate matter can lead to vascular endothelial injury, systemic inflammation, atherosclerosis, and microvascular changes,\cite{Sun2005,Chow2006} and thus may cause urine volume decreases, which can result in urolithiasis. However, there are as yet no studies examining the correlation between urolithiasis and ambient air pollution, which bears further investigation.

Our study has limitations. First, as in most previous studies, we used fixed-site monitor measurements to represent personal exposure, causing exposure errors. However, the resultant non-differential error was reported to produce an underestimate of the correlations of ambient air pollution.\cite{Samet2000} Second, due to data limitations, we didn’t take pre-existing diseases and unhealthy factors into account, either of which may weaken one’s tolerance of air pollutants. Third, since our study was conducted only from emergency department data, some visits could not produce a definite diagnosis, or even get a wrong diagnosis, which is hard to avoid. Fourth, this study collected data from only one highly polluted city, thus its general application might be limited.

**Conclusions**

Our time-series study suggests that ambient air pollution (especially CO and $O_3$) has a positive correlation with the ERVs for abdominal pain in Wuhan, China. The effects varied by season, gender and age. The estimates of effects from most pollutants on ERVs for abdominal pain were higher among females and younger people. The correlations between PM$_{2.5}$, PM$_{10}$ and ERVs for abdominal pain were stronger in cool seasons while the correlation of CO was higher in warm seasons. Specifically, we focused more attention on the correlations between ambient air pollution and specific emergency diseases manifested as abdominal pain, and we expect this study can help hospitals to take precaution in polluted days, and improve timely treatment in hospitals.

**Declarations**

**Ethics approval and consent to participate**

The research protocol was approved by the Medical Ethics Committee of Zhongnan Hospital. (IRB number: 2021018K)

**Consent for publication**

Not applicable

**Availability of data and materials**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

**Competing interests**

The authors declare that they have no competing interests

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Authors’ contributions

Yaqi Liu: Methodology, Software, Investigation, Visualization, Writing - Original Draft. Yi Jiang: Writing- Reviewing and Editing. Manyi Wu: Investigation. Sunghar Muheyat: Software, Validation. Dongai Yao: Resources, Xiaoqing Jin: Supervision, Project administration, Funding acquisition.

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Figures
Figure 1

Wuhan (shaded area is the urban area)
Figure 2

Spearman correlations among exposure variables in Wuhan, China (2016-2018). temp, Temperature; rhum, Relative Humidity
Figure 3

Percentage change (%) of ERVs for abdominal pain (mean and 95% CI) associated with a 10 μg/m3 increase in various air pollutant concentrations using different lag structures.
The exposure-response (E-R) curves

**Figure 4**

The exposure-response relationship curves of SO2 (lag01), NO2 (lag06), PM2.5 (lag07), PM 10 (lag06), CO (lag06) and O3 (lag01)

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