Original Article

Acute effects of air pollutants on daily mortality and hospitalizations due to cardiovascular and respiratory diseases

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Background: Chiang Dao is one of the districts in Chiang Mai, Thailand facing high level of seasonal air pollution every year, the exposure of community dwellers to outdoor air pollutants 24 hours a day during seasonal smog period because of their open-air housing style, and agricultural occupational hazard. In addition, Chiang Dao hospital is the only available hospital serving the community with open-air wards; therefore we could certainly to identify the association between air pollution and mortality of hospitalized patients. Thus, the aim of this study was to determine the association between daily average seasonal air pollutants and daily mortality of hospitalized patients and community dwellers as well as emergency and hospitalization visits for serious respiratory, cardiovascular, and cerebrovascular diseases.

Methods: This time series study was conducted between 1 March 2016 and 31 March 2017. The association of various air pollutant concentrations including particulate matter diameter less than 10 and 2.5 microns (PM_{10} and $PM_{2.5}$), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO), ozone (O_3) and daily mortality of hospitalized patients and community dwellers as well as relationship with frequencies of serious respiratory, cardiovascular, and cerebrovascular diseases were analyzed using a general linear model with Poisson distribution.

Results: Only $PM_{2.5}$ was found to be associated with increased daily mortality of hospitalized patients (lag day 6, adjusted RR =1.153, 95% CI: 1.001–1.329), whereas PM_{10}, $PM_{2.5}$, NO_2, and O_3 were associated with increased daily non-accidental mortality of community dwellers (lag day 0–7, adjusted RR =1.006–1.040, 95% CI: 1.000–1.074). For acute serious respiratory events; PM_{10} and $PM_{2.5}$ were associated with acute exacerbation of chronic obstructive pulmonary disease (AECOPD), while SO_2, CO, and O_3 were associated with emergency visits for community-acquired pneumonia (CAP). O_3 was associated with emergency visits for heart failure (HF), NO_2 with emergency visits for myocardial infarction (MI), and SO_2 with hospitalized visits for cerebrovascular accident (CVA).

Conclusions: Seasonal air pollutants were found to be associated with higher mortality among hospitalized patients and community dwellers with varying effects on severe acute respiratory, cardiovascular, and cerebrovascular diseases.

Keywords: Lung diseases; heart diseases; air pollution; hospitalization; mortality

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Introduction

Air pollution is becoming an increasing concern around the world. Several reports have shown associations between acute or chronic exposure to air pollution and morbidity or mortality (1-3). Previous studies have shown association between ambient air pollution exposure and clinical events such as emergency visit, hospital admission for respiratory diseases (4-11), cardiovascular diseases (7,12-19), and cerebrovascular diseases (20). In addition, a number of studies have shown a connection between ambient air pollution exposure and non-accidental mortality (21-26).

The relationship between air pollution and detrimental health effect in Chiang Mai province located in northern Thailand has been recognized for more than a decade. However, only two studies documenting the negative impact of air pollution on health have been published (27,28). The association between ambient air pollutants including nitrogen dioxide (NO_2), sulfur dioxide (SO_2), particulate matters less than 10 microns (PM_{10}) with decreased lung function measured by peak expiratory flow rate (PEFR) was found in asthma patients (27). Another study revealed the association between PM_{10} and exacerbations of chronic obstructive pulmonary disease (COPD) and asthma (28). In our study subjects who lived only in the metropolitan area of Chiang Mai province were included and not those from the rural regions of northern Thailand that were more seriously affected by seasonal air pollution caused by agricultural farm burnings and forest fires. Most of the housing style of community dwellers in rural area is open-air houses without built-in air conditioners or air purifiers. This allows the outdoor air to be almost the same as indoor air in terms of particulate content. Chiang Dao district is one of the rural communities located in the north of Chiang Mai approximately 770 kilometers from Bangkok. It covers an area of approximately 1,882 km^2 and is surrounded by high mountain range. Besides, the vast majority of rural dwellers are farmers or gardeners. There is around 90,000 Chiang Dao dwellers distributed among 7 administrative sub-districts with only one single 60 bed-community serve the health needs of local dwellers. All wards of this community hospital are open-air style buildings unequipped with air conditioners or air purifier systems exposing the patients to outdoor air pollutants in the same way as their houses. Chiang Dao, like all districts in Chiang Mai, has been facing seasonal air pollution from January to April annually for the past decade. The daily average level of PM_{10} has been recorded to reach above 50 micrograms per cubic meter (μg)/m^3 more than one third of each preceding year (28).

We selected Chiang Dao district for this study based on several reasons; it is one of the districts in Chiang Mai facing high level of seasonal air pollution every year, its geographical features surrounded by mountain ranges, the exposure of community dwellers to outdoor air pollutants 24 hours a day during seasonal smog period because of their open-air housing style, and agricultural occupational hazard. In addition, Chiang Dao hospital is the only available hospital serving the community with open-air wards; therefore we could certainly to identify the association between air pollution and mortality of hospitalized patients. Our first objective is to determine the association between air pollutants and mortality of hospitalized patients and community dwellers. The second objective is to determine the associations between air pollutants and both emergency and hospitalization visits for acute serious respiratory, cardiovascular, and cerebrovascular events in the study population.

Methods

Design and study participants

A time series study was conducted between March 2016 and March 2017 in Chiang Dao district, Chiang Mai, Thailand. The ICD-10 registry records, collected from Chiang Dao hospital for daily emergency- and hospitalization visits due to acute respiratory (acute exacerbation of chronic obstructive pulmonary disease and community-acquired pneumonia, AECOPD and CAP), acute cardiovascular events (acute myocardial infarction and congestive heart failure, MI and HF), and acute cerebrovascular events (hemorrhagic and ischemic strokes, cerebrovascular accident, CVA) were reviewed and adjudicated by at least two physicians in the study team and one physician of Chiang Dao hospital. In addition the daily numbers of emergency and hospitalization visits due to AECOPD, CAP, MI, HF, and CVA were recorded by the physicians on duty in the emergency room with the primary diagnoses based on the International Classification of Diseases (ICD) version 10 (ICD-10 J44.1, J18, I21, I50, and I63 for AECOPD, CAP, MI, HF, and CVA, respectively). These data were reviewed and adjudicated by a dedicated physician team from the emergency room, a pulmonologist, and a cardiologist in the study team based on ICD-10. A special permission was received to extract data on daily deaths of hospitalized

Table 1 Daily pollutants data, meteorological parameters (from March 2016 to March 2017)

Pollutants and meteorological data	Median	Interquartile range
Type of pollutants		
PM_{10} (μg/m^3)	37.36	26.23–62.54
$PM_{2.5}$ (μg/m^3)	20.42	12.62–42.96
SO_2 (μg/m^3)	2.62	2.62–3.07
NO_2 (μg/m^3)	27.92	22.24–41.77
CO (μg/m^3)	1,130.00	970.00–1,317.50
O_3 (μg/m^3)	40.39	29.16–68.57
Meteorological parameters		
Temperature (c)	20.35	14.58–34.28
Rain (mm)	0.00	0.00–3.15
Pressure (hpa)	1,006.60	1,004.70–1,010.28
Humidity (%)	83.00	48.00–92.00
Wind speed (km/hr)	31.51	22.24–40.77
Humidity (%)	83.00	48.00–92.00
Wind speed (km/hr)	31.51	22.24–40.77

PM_{10}, particulate matters with diameter of less than 10 micron; $PM_{2.5}$, particulate matters with diameter of less than 2.5 micron; CO, carbon monoxide; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; O_3, ozone.

patients and community dwellers (excluding accidental and suicidal deaths) of Chiang Dao district from the Registry of hospital deaths and from the Office of certification and registration of local deaths. The study was approved by the Ethics Committee of the Faculty of Medicine, Chiang Mai University (Study code: MED-2558-03032, Date approval: 14th December 2015).

Measurements of air pollutants and meteorological parameters

Sampling station was located in Chiang Dao hospital, Chiang Mai, Thailand. Ambient air concentration of pollutants was measured by the DustDETECT™. The analytical method for PM was specifically designed to monitor the flow of particulate emissions from small stacks and emission points being passed through an air filtration system. The data reported were daily maximum, minimum, and average concentrations for PM_{10}, $PM_{2.5}$, SO_2, NO_2, carbon monoxide (CO), and ozone (O_3). The unit of the air pollutants was μg/m^3. The meteorological data including temperature, relative humidity, rainfall, wind speed, and pressure from the meteorology monitoring stations in Chiang Dao district can be obtained from the meteorological department website at https://meteorology.hrdi.or.th.

Statistical analysis

Results for numerical values were expressed as means ± SD or median, IQR (Interquartile range) and those for categorical data were expressed as absolute frequencies and percentages. The association between daily average concentrations of air pollutants and daily deaths of hospitalized patients and community dwellers, as well as the incidence of AECOPD, CAP, MI, HF, and CVA were analyzed using the application of general linear models with Poisson distribution, a method of analysis which has performed reliably and satisfactorily in previous studies (27,28). Poisson models with log links are often called log-linear models and are used for frequency data. To find out the association between the effect of air pollutants on disease exacerbation, Poisson regression was used for analysis after adjustment for the temperature, wind speed, pressure, rainfall and relative humidity. To assess the lag structure between concentrations of air pollutants and deaths of hospitalized patients and community dwellers as well as emergency and hospitalization visits of serious respiratory, cardiovascular, and cerebrovascular events, we initially examined separate models for each lag from 0 to 7 days prior to the deaths or visits. The lag time zero (lag 0) was defined as the day of air pollutants measurement. Finally, risk regression analysis was applied to the data in order to estimate relative risk (RR) with 95% confidence intervals (CI) of the independent variables in the constructed model. The adjusted RRs were estimated with each 10 μg/m^3 increment of $PM_{2.5}$, PM_{10}, and CO, each 1 μg/m^3 increment of NO_2, and O_3, and each 0.1 μg/m^3 increment of SO_2. All analyses were carried out with the SPSS statistical package, version 22 for IBM (SPSS Inc., IL, USA).

Results

The daily pollutants data including PM_{10}, $PM_{2.5}$, SO_2, NO_2, CO, O_3, and meteorological parameters are shown in *Table 1*. Concentrations of all air pollutants were maximal in March of both years (2016 and 2017). The daily variations of each pollutant throughout the study year were shown in *Figure 1*.

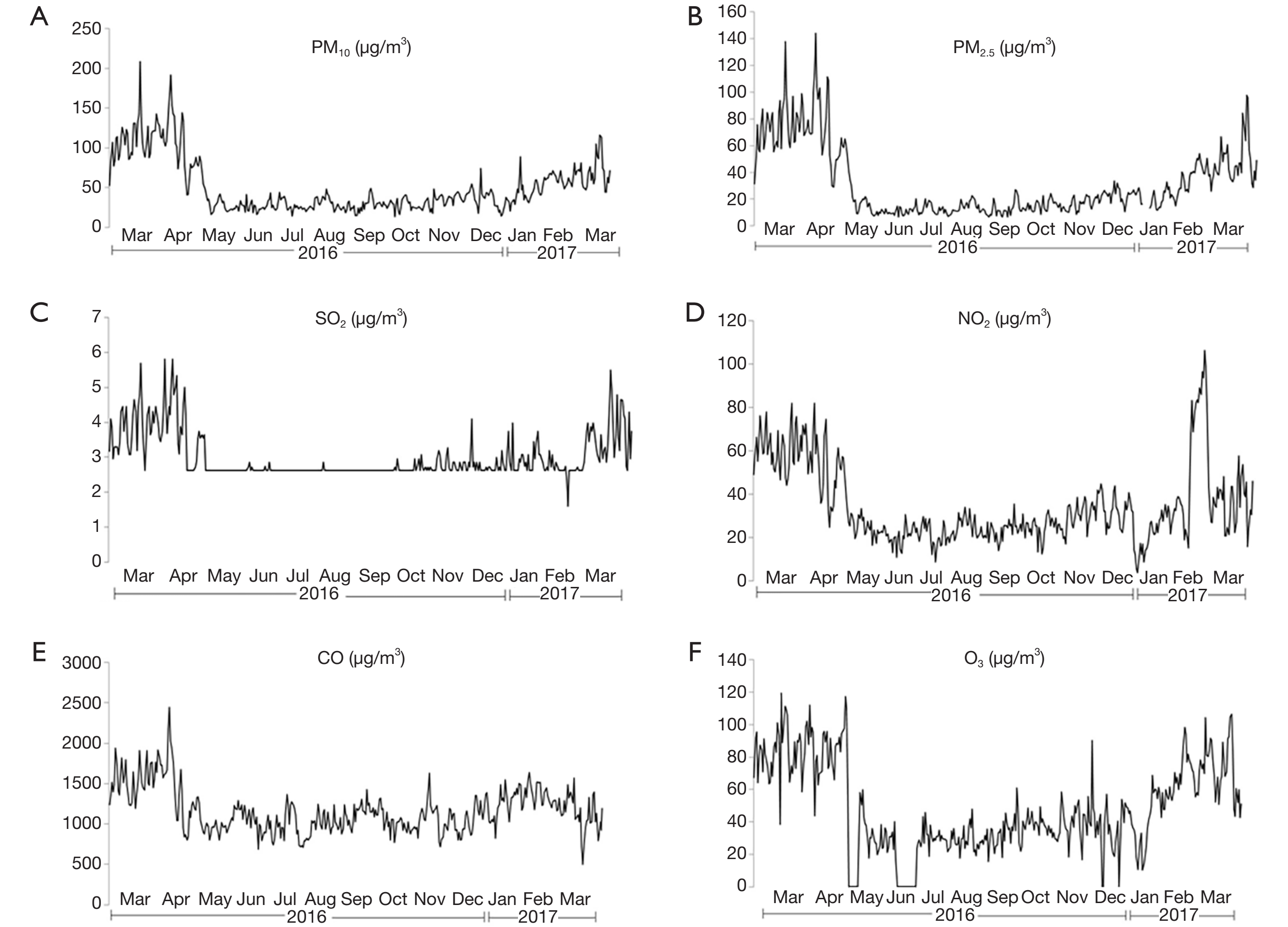

Figure 1 Variation of each air pollutant throughout the study year (March 2016–March 2017). (A) PM_{10}; (B) $PM_{2.5}$; (C) SO_2; (D) NO_2; (E) CO; (F) O_3. PM_{10}, particulate matters with diameter of less than 10 micron; $PM_{2.5}$, particulate matters with diameter of less than 2.5 micron; CO, carbon monoxide; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; O_3, ozone.

Deaths of hospitalized patients and non-accidental deaths of community dwellers are shown in *Table 2*. After screening a total of 4,685 visits (3,009 and 1,676 for emergency and hospitalization visit, respectively) at the Chiang Dao hospital between March 2016 and March 2017, total emergency visits of 2,419 and 590 patients with acute respiratory, cardiovascular and cerebrovascular events were included for analysis. The most common of acute respiratory event was upper respiratory tract infection (URI) and the one for acute cardiovascular and cerebrovascular events was acute hypertension (HT). Total hospitalization admissions of 1,676 emergencies (817 for acute respiratory and 859 for cardiovascular and cerebrovascular events) were included for analysis (*Table 2*). Acute serious respiratory events were defined as AECOPD and CAP and acute serious cardiovascular and cerebrovascular events were defined as MI, HF and CVA in this study.

After adjustment for temperature, relative humidity, rainfall, wind speed, and pressure, the association between air pollutants and deaths of hospitalized patients and community dwellers are shown in *Table 3*. $PM_{2.5}$, PM_{10}, NO_2 and O_3 were found to have a positive association with daily mortality of community dwellers on different lag days but only $PM_{2.5}$ had a positive association with daily mortality of hospitalized patients (adjusted RR =1.153; 95% CI: 1.001–1.329). The associations between each of air pollutants (PM_{10}, $PM_{2.5}$, SO_2, NO_2, CO, O_3) and emergency and hospitalization visits of AECOPD, CAP, MI, HF, and

Table 2 Descriptive summary for the study period (March 2016–March 2017), emergency and hospitalization visits for acute respiratory diseases, cardiovascular diseases, and hospital and non-accidental deaths

Daily	Total	Mean ± SD	Median (IQR)	Range
Emergency visits				
COPD	380	0.96±0.98	1 (0–2)	0–5
Bronchitis	234	0.59±0.81	0 (0–1)	0–5
Upper respiratory tract infection	1,486	3.75±4.51	3 (2–5)	0–44
Community acquired pneumonia	319	0.81±1.01	1 (0–1)	0–5
Hypertension	237	0.60±0.77	0 (0–1)	0–4
Heart failure	102	0.26±0.54	0 (0–0)	0–4
Myocardial infarction	30	0.08±0.26	0 (0–0)	0–1
Stroke	221	0.56±0.79	0 (0–1)	0–4
Hospitalization				
COPD	335	0.85±0.94	1 (0–1)	0–5
Upper respiratory tract infection	157	0.40±0.65	0 (0–1)	0–3
Community acquired pneumonia	325	0.82±1.06	0.5 (0–1)	0–5
Hypertension	298	0.75±1.07	0 (0–1)	0–5
Heart failure	223	0.56±0.84	0 (0–1)	0–4
Myocardial infarction	53	0.13±0.45	1 (0–0)	0–4
Stroke	285	0.72±1.00	1 (0–1)	0–6
Hospital death	68	0.17±0.59	0 (0–0)	0–5
Non-accidental death	477	1.20±1.17	1 (0–2)	0–7

COPD, chronic obstructive pulmonary disease.

CVA on different lag days are shown in *Tables 4*-7. For acute serious respiratory events, $PM_{2.5}$ and PM_{10} had a positive association with both emergency and hospitalized visits of AECOPD while SO_2, CO, O_3 had a positive association with emergency visits of CAP only (*Table 4*). For acute serious cardiovascular events, NO_2 and O_3 also had a positive association with emergency visits, but not with hospitalization visits of MI and HF (*Tables 5* and 7). Only SO_2 had a positive association with CVA (*Table* 7).

Discussion

This prospective epidemiologic time-series study in a single community with documented exposure to seasonal air pollution revealed the association between air pollutants and daily mortality of hospitalized patients and community dwellers, as well as differential effects of air pollutants on acute serious respiratory (AECOPD and CAP), cardiovascular (MI and HF) and cerebrovascular (CVA) events requiring emergency and/or hospitalization visits soon after exposure.

The relationship between increased concentrations of air pollutants and non accidental mortality of population which has been well documented worldwide (21-26), was reconfirmed in this study. However the association has never been studied during seasonal air pollution period as in our study in northern Thailand. Moreover, the study revealed that short term exposure to $PM_{2.5}$ increased the relative risk of daily mortality of hospitalized patients by 15.3% per 10 $\mu g/m^3$ (lag day 6, relative risk =1.153, 95% CI: 1.001–1.329) which to the best of our knowledge, this is the first time-series study of air pollution which demonstrated the association of air pollutant with daily mortality of hospitalized patients. The relative risk of $PM_{2.5}$ associated with daily mortality of hospitalized patients in our study was found to be 4.4-fold higher than that of community dwellers

Table 3 Associations between air pollutants and non-accidental death

Outcomes	PM_{10}	$PM_{2.5}$	SO_2	NO_2	CO	O_3
Hospital death						
lag 0	1.027 (0.929–1.134)	0.983 (0.859–1.126)	0.975 (0.912–1.041)	0.986 (0.960–1.013)	0.996 (0.983–1.010)	1.012 (0.996–1.028)
lag 1	0.964 (0.872–1.066)	0.950 (0.832–1.085)	0.940 (0.869–1.017)	0.987 (0.960–1.015)	1.009 (0.994–1.024)	1.003 (0.988–1.018)
lag 2	0.948 (0.852–1.055)	0.908 (0.777–1.061)	0.956 (0.884–1.034)	0.986 (0.957–1.016)	1.009 (0.994–1.024)	0.990 (0.976–1.005)
lag 3	1.025 (0.961–1.094)	1.067 (0.909–1.253)	1.031 (0.965–1.100)	0.991 (0.964–1.019)	1.010 (0.996–1.024)	0.995 (0.980–1.010)
lag 4	1.009 (0.941–1.081)	0.994 (0.906–1.092)	1.028 (0.997–1.060)	1.016 (0.992–1.041)	1.006 (0.998–1.014)	0.982 (0.959–1.005)
lag 5	0.982 (0.911–1.059)	0.976 (0.885–1.076)	1.022 (0.951–1.099)	0.999 (0.975–1.024)	1.003 (0.995–1.012)	0.992 (0.977–1.007)
lag 6	1.083 (0.972–1.207)	1.153 (1.001–1.329)*	0.921 (0.845–1.004)	0.974 (0.946–1.002)	1.004 (0.990–1.018)	0.979 (0.965–0.993)
lag 7	1.007 (0.938–1.081)	1.012 (0.923–1.109)	0.979 (0.906–1.058)	0.992 (0.968–1.017)	1.014 (1.000–1.029)	0.982 (0.968–0.996)
Non-accidental death						
lag 0	1.003 (0.963–1.044)	0.989 (0.935–1.046)	1.005 (0.982–1.028)	1.000 (0.992–1.008)	1.000 (0.995–1.005)	1.006 (1.001–1.011)*
lag 1	1.008 (0.968–1.049)	1.012 (0.958–1.070)	1.018 (0.994–1.042)	1.004 (0.996–1.012)	1.004 (0.999–1.009)	1.002 (0.997–1.008)
lag 2	0.983 (0.943–1.024)	0.973 (0.919–1.030)	1.009 (0.986–1.032)	1.003 (0.995–1.010)	1.002 (0.999–1.006)	1.007 (1.001–1.012)*
lag 3	0.999 (0.959–1.040)	0.993 (0.939–1.050)	1.006 (0.983–1.030)	1.007 (1.000–1.015)	1.002 (0.998–1.005)	1.003 (0.998–1.009)
lag 4	1.022 (0.983–1.063)	1.028 (0.974–1.085)	0.998 (0.974–1.022)	1.008 (1.001–1.015)*	1.002 (0.999–1.006)	1.000 (0.994–1.005)
lag 5	1.027 (0.988–1.069)	1.029 (0.980–1.080)	0.996 (0.972–1.020)	1.007 (1.000–1.015)	1.001 (0.996–1.006)	1.000 (0.994–1.005)
lag 6	1.030 (1.004–1.056)*	1.035 (1.002–1.070)*	1.014 (0.991–1.038)	1.009 (1.001–1.017)*	0.998 (0.993–1.003)	0.998 (0.993–1.004)
lag 7	1.030 (1.004–1.056)*	1.040 (1.006–1.074)*	1.003 (0.978–1.028)	1.002 (0.994–1.011)	0.998 (0.993–1.003)	0.995 (0.990–1.000)

Data are adjusted RR (95% CI). RR, relative risk; *, statistical significance level <0.05.

Table 4 Associations between air pollutants and emergency visits for serious respiratory diseases

Outcomes	PM_{10}	$PM_{2.5}$	SO_2	NO_2	CO	O_3
COPD						
lag 0	1.116 (1.026–1.213)*	1.074 (0.963–1.197)	0.969 (0.943–0.996)	0.999 (0.990–1.008)	1.002 (0.996–1.008)	0.998 (0.992–1.004)
lag 1	1.088 (1.001–1.184)*	1.124 (1.030–1.227) *	0.977(0.951–1.004)	0.995 (0.986–1.005)	1.003 (0.997–1.009)	0.998 (0.992–1.004)
lag 2	1.074 (0.987–1.169)	1.054 (0.946–1.175)	0.988 (0.962–1.016)	0.998 (0.988–1.007)	1.003 (0.997–1.009)	0.997 (0.991–1.003)
lag 3	1.037 (0.953–1.128)	0.999 (0.902–1.106)	1.016 (0.991–1.043)	0.997 (0.988–1.007)	0.999 (0.993–1.005)	1.002 (0.995–1.008)
lag 4	1.009 (0.929–1.096)	0.965 (0.873–1.067)	1.020 (0.994–1.047)	1.004 (0.995–1.014)	1.000 (0.994–1.005)	0.998 (0.992–1.004)
lag 5	0.994 (0.915–1.079)	0.925 (0.836–1.023)	1.020 (0.994–1.047)	1.005 (0.996–1.015)	1.002 (0.996–1.008)	0.997 (0.990–1.003)
lag 6	1.020 (0.940–1.106)	0.968 (0.877–1.068)	1.003 (0.975–1.031)	1.002 (0.992–1.011)	1.002 (0.997–1.008)	0.994 (0.988–1.000)
lag 7	1.015 (0.934–1.103)	0.980 (0.887–1.082)	1.003 (0.976–1.031)	0.997 (0.988–1.007)	1.004 (0.998–1.010)	0.999 (0.993–1.006)
Community acquired pneumonia						
lag 0	0.935 (0.872–1.003)	0.907 (0.832–0.987)	0.825 (0.610–1.115)	1.001 (0.991–1.010)	1.007 (1.001–1.014)*	1.007 (1.001–1.015)*
lag 1	0.922 (0.857–0.991)	0.873 (0.795–0.960)	1.015 (0.986–1.044)	1.001 (0.991–1.011)	1.008 (1.002–1.015)*	1.011 (1.003–1.018)*
lag 2	0.920 (0.855–0.989)	0.911 (0.830–1.000)	0.992 (0.963–1.022)	1.000 (0.990–1.009)	1.007 (1.001–1.014)*	1.009 (1.002–1.016)*
lag 3	0.930 (0.870–0.995)	0.911 (0.835–0.994)	0.969 (0.939–1.000)	0.998 (0.989–1.008)	1.007 (1.001–1.013)*	1.006 (0.999–1.013)
lag 4	0.994 (0.944–1.046)	0.982 (0.921–1.046)	0.993 (0.964–1.023)	0.997 (0.987–1.007)	1.002 (0.996–1.009)	1.003 (0.995–1.010)
lag 5	0.961 (0.912–1.012)	0.947 (0.888–1.009)	1.023 (0.993–1.053)	1.007 (0.997–1.017)	1.007 (1.000–1.013)	1.005 (0.998–1.013)
lag 6	0.996 (0.964–1.029)	0.992 (0.950–1.036)	1.038 (1.009–1.067)*	1.006 (0.996–1.016)	1.006 (1.000–1.012)	1.011 (1.004–1.018)*
lag 7	1.004 (0.972–1.037)	0.999 (0.957–1.042)	1.014 (0.984–1.045)	0.998 (0.988–1.009)	1.006 (1.000–1.012)	1.006 (0.999–1.014)

Data are adjusted RR (95% CI). RR, relative risk; *, statistical significance level <0.05.

Table 5 Association between air pollutants and emergency visits for serious cardiovascular and cerebrovascular diseases

Outcomes	PM_{10}	$PM_{2.5}$	SO_2	NO_2	CO	O_3
Heart failure						
lag 0	0.997 (0.940–1.057)	0.988 (0.914–1.067)	0.978 (0.925–1.034)	0.998 (0.981–1.016)	1.005 (0.994–1.016)	1.005 (0.992–1.017)
lag 1	1.001 (0.944–1.060)	0.987 (0.914–1.067)	1.007 (0.956–1.061)	0.998 (0.979–1.017)	0.999 (0.989–1.010)	1.000 (0.988–1.012)
lag 2	1.007 (0.951–1.066)	0.997 (0.924–1.075)	0.992 (0.942–1.044)	1.002 (0.985–1.021)	0.990 (0.979–1.001)	0.995 (0.984–1.007)
lag 3	1.008 (0.950–1.070)	1.002 (0.925–1.084)	1.006 (0.958–1.056)	1.006 (0.989–1.023)	0.991 (0.981–1.002)	1.006 (0.994–1.018)
lag 4	0.981 (0.923–1.042)	0.957 (0.882–1.039)	0.986 (0.937–1.039)	1.003 (0.986–1.020)	0.995 (0.984–1.006)	1.014 (1.002–1.027)*
lag 5	0.975 (0.917–1.037)	0.969 (0.894–1.049)	0.954 (0.899–1.011)	0.990 (0.972–1.009)	0.997 (0.985–1.008)	1.003 (0.991–1.015)
lag 6	1.003 (0.947–1.062)	1.002 (0.930–1.079)	0.987 (0.935–1.042)	0.995 (0.978–1.013)	1.003 (0.992–1.014)	1.007 (0.995–1.019)
lag 7	0.996 (0.940–1.056)	0.992 (0.919–1.070)	1.007 (0.955–1.063)	1.000 (0.983–1.018)	1.003 (0.992–1.014)	1.003 (0.991–1.016)
Myocardial infarction						
lag 0	1.015 (0.916–1.125)	1.035 (0.909–1.179)	0.922 (0.831–1.023)	1.012 (0.985–1.038)	0.987 (0.965–1.009)	0.993 (0.973–1.014)
lag 1	1.030 (0.933–1.137)	1.050 (0.926–1.192)	0.969 (0.879–1.068)	1.021 (0.996–1.047)	0.988 (0.967–1.009)	0.991 (0.970–1.012)
lag 2	0.957 (0.838–1.093)	0.970 (0.817–1.152)	1.032 (0.939–1.135)	1.036 (1.011–1.060)*	0.992 (0.972–1.012)	0.977 (0.958–0.998)
lag 3	0.973 (0.851–1.113)	1.007 (0.847–1.196)	1.018 (0.930–1.113)	1.030 (1.006–1.055)*	0.984 (0.964–1.004)	0.983 (0.964–1.004)
lag 4	0.974 (0.852–1.114)	0.994 (0.836–1.183)	0.967 (0.880–1.063)	1.020 (0.996–1.045)	0.989 (0.968–1.011)	0.993 (0.972–1.014)
lag 5	1.044 (0.948–1.150)	1.073 (0.949–1.213)	0.980 (0.889–1.081)	1.017 (0.992–1.044)	0.995 (0.974–1.017)	0.998 (0.976–1.020)
lag 6	1.045 (0.949–1.151)	1.078 (0.954–1.218)	0.987 (0.892–1.091)	1.014 (0.987–1.042)	0.997 (0.976–1.019)	0.993 (0.972–1.014)
lag 7	1.036 (0.939–1.143)	1.067 (0.943–1.208)	0.999 (0.902–1.107)	1.019 (0.993–1.046)	1.000 (0.979–1.022)	0.994 (0.973–1.016)
Stroke						
lag 0	1.007 (0.949–1.069)	1.026 (0.951–1.108)	1.030 (0.998–1.064)	1.006 (0.994–1.018)	0.997 (0.992–1.002)	0.997 (0.989–1.005)
lag 1	1.012 (0.953–1.074)	1.031 (0.954–1.113)	0.995 (0.960–1.030)	1.002 (0.990–1.014)	0.997 (0.992–1.002)	0.997 (0.989–1.005)
lag 2	0.999 (0.942–1.058)	1.015 (0.942–1.094)	1.015 (0.982–1.050)	1.007 (0.996–1.019)	0.999 (0.994–1.004)	0.998 (0.991–1.006)
lag 3	1.016 (0.958–1.078)	1.048 (0.972–1.130)	0.964 (0.929–1.000)	1.000 (0.988–1.011)	0.998 (0.993–1.003)	0.996 (0.989–1.004)
lag 4	1.009 (0.952–1.070)	1.019 (0.945–1.098)	0.987 (0.954–1.022)	1.000 (0.989–1.012)	0.999 (0.995–1.004)	1.008 (1.000–1.016)
lag 5	1.014 (0.957–1.075)	1.043 (0.968–1.125)	0.994 (0.960–1.029)	1.000 (0.989–1.012)	1.000 (0.995–1.005)	1.004 (0.996–1.012)
lag 6	1.026 (0.969–1.087)	1.063 (0.988–1.145)	0.995 (0.961–1.030)	1.000 (0.988–1.012)	1.000 (0.995–1.005)	1.002 (0.995–1.010)
lag 7	1.001 (0.947–1.059)	1.003 (0.933–1.079)	1.007 (0.973–1.042)	1.007 (0.996–1.018)	1.002 (0.998–1.007)	1.004 (0.996–1.012)

Data are adjusted RR (95% CI). RR, relative risk; *, statistical significance level <0.05.

Table 6 Association between air pollutants and hospitalization for serious respiratory diseases

Outcomes	PM_{10}	$PM_{2.5}$	SO_2	NO_2	CO	O_3
COPD						
lag 0	1.002 (0.938–1.072)	1.015 (0.958–1.076)	0.964 (0.935–0.993)	1.001 (0.992–1.010)	1.004 (0.998–1.010)	1.000 (0.994–1.006)
lag 1	0.995 (0.929–1.065)	0.982 (0.904–1.068)	0.975 (0.945–1.005)	1.001 (0.992–1.011)	1.004 (0.997–1.010)	0.998 (0.991–1.004)
lag 2	0.992 (0.927–1.062)	1.001 (0.923–1.086)	0.975 (0.946–1.005)	1.000 (0.990–1.010)	1.003 (0.997–1.010)	0.996 (0.990–1.003)
lag 3	1.053 (1.023–1.085)*	1.059 (1.015–1.104)*	0.981 (0.952–1.011)	0.997 (0.987–1.007)	0.999 (0.993–1.006)	1.002 (0.995–1.009)
lag 4	1.027 (0.990–1.065)	1.030 (0.982–1.080)	0.989 (0.960–1.018)	1.001 (0.992–1.011)	1.000 (0.994–1.007)	1.000 (0.993–1.006)
lag 5	1.008 (0.955–1.064)	1.002 (0.934–1.074)	1.019 (0.991–1.048)	1.005 (0.995–1.015)	1.003 (0.997–1.009)	1.002 (0.995–1.008)
lag 6	1.002 (0.949–1.059)	1.007 (0.939–1.081)	0.996 (0.967–1.026)	1.004 (0.994–1.014)	1.002 (0.996–1.009)	0.999 (0.992–1.005)
lag 7	1.006 (0.957–1.057)	1.022 (0.958–1.089)	1.002 (0.973–1.032)	1.004 (0.995–1.014)	1.003 (0.996–1.009)	1.001 (0.994–1.007)
Community acquired pneumonia						
lag 0	1.001 (0.969–1.034)	1.004 (0.963–1.047)	0.998 (0.969–1.028)	0.999 (0.989–1.009)	0.999 (0.995–1.004)	0.999 (0.992–1.005)
lag 1	1.007 (0.974–1.041)	1.015 (0.972–1.059)	1.002 (0.973–1.032)	0.998 (0.988–1.008)	1.001 (0.997–1.005)	1.006 (0.999–1.012)
lag 2	0.999 (0.967–1.032)	1.002 (0.961–1.045)	1.001 (0.972–1.032)	1.003 (0.994–1.013)	1.001 (0.997–1.005)	1.003 (0.996–1.010)
lag 3	1.000 (0.968–1.033)	1.000 (0.959–1.043)	0.981 (0.950–1.012)	1.001 (0.991–1.011)	1.000 (0.996–1.004)	0.998 (0.991–1.004)
lag 4	0.995 (0.963–1.028)	1.003 (0.962–1.045)	1.004 (0.974–1.034)	1.000 (0.990–1.010)	0.999 (0.995–1.003)	1.000 (0.993–1.007)
lag 5	0.994 (0.962–1.028)	0.993 (0.952–1.036)	1.008 (0.979–1.037)	0.999 (0.989–1.009)	0.999 (0.994–1.003)	1.004 (0.997–1.011)
lag 6	0.990 (0.958–1.024)	0.992 (0.950–1.035)	1.026 (0.997–1.056)	1.001 (0.991–1.012)	0.999 (0.995–1.003)	1.003 (0.996–1.010)
lag 7	0.992 (0.957–1.028)	0.995 (0.950–1.042)	1.007 (0.976–1.039)	1.000 (0.990–1.011)	1.001 (0.997–1.005)	1.001 (0.994–1.008)

Data are adjusted RR (95% CI). RR, relative risk; *, statistical significance level <0.05.

Table 7 Association between air pollutants and hospitalization for serious cardiovascular and cerebrovascular diseases

Outcomes	PM_{10}	$PM_{2.5}$	SO_2	NO_2	CO	O_3
Heart failure						
lag 0	0.966 (0.925–1.008)	0.952 (0.900–1.007)	0.988 (0.967–1.010)	1.001 (0.993–1.008)	0.997 (0.992–1.002)	0.999 (0.994–1.003)
lag 1	0.965 (0.924–1.007)	0.947 (0.895–1.003)	0.989 (0.968–1.011)	1.000 (0.993–1.007)	0.996 (0.991–1.001)	0.998 (0.994–1.003)
lag 2	0.984 (0.903–1.072)	1.004 (0.906–1.113)	0.986 (0.950–1.024)	1.001 (0.994–1.008)	0.999 (0.991–1.006)	0.997 (0.992–1.002)
lag 3	1.002 (0.930–1.080)	0.991 (0.900–1.090)	0.977 (0.940–1.015)	1.000 (0.993–1.007)	0.996 (0.991–1.001)	0.997 (0.992–1.002)
lag 4	1.006 (0.924–1.096)	0.987 (0.890–1.095)	0.983 (0.947–1.021)	0.996 (0.989–1.004)	0.996 (0.988–1.003)	0.998 (0.993–1.003)
lag 5	1.045 (0.953–1.145)	1.097 (0.985–1.222)	0.975 (0.939–1.012)	0.995 (0.987–1.003)	0.997 (0.989–1.005)	0.999 (0.994–1.003)
lag 6	1.001 (0.954–1.051)	1.012 (0.951–1.077)	0.989 (0.968–1.010)	0.999 (0.991–1.006)	0.999 (0.994–1.004)	1.000 (0.995–1.005)
lag 7	1.003 (0.961–1.047)	1.005 (0.950–1.063)	1.000 (0.980–1.020)	1.001 (0.993–1.008)	0.999 (0.994–1.004)	1.000 (0.995–1.005)
Myocardial infarction						
lag 0	0.982 (0.903–1.069)	0.974 (0.873–1.087)	0.979 (0.904–1.061)	1.007 (0.984–1.030)	0.999 (0.989–1.009)	0.996 (0.980–1.013)
lag 1	0.975 (0.895–1.063)	0.990 (0.890–1.101)	0.930 (0.855–1.011)	0.997 (0.973–1.021)	0.995 (0.985–1.006)	0.998 (0.983–1.014)
lag 2	0.997 (0.919–1.081)	1.007 (0.908–1.116)	0.982 (0.906–1.064)	1.007 (0.983–1.032)	0.998 (0.987–1.008)	0.983 (0.968–0.998)
lag 3	0.990 (0.912–1.075)	0.984 (0.884–1.096)	1.008 (0.932–1.090)	1.018 (0.995–1.041)	0.998 (0.988–1.008)	0.992 (0.981–1.002)
lag 4	0.977 (0.897–1.064)	0.990 (0.891–1.101)	0.947 (0.871–1.029)	1.010 (0.988–1.033)	0.994 (0.984–1.005)	0.987 (0.972–1.002)
lag 5	0.969 (0.888–1.058)	0.964 (0.861–1.079)	0.977 (0.903–1.056)	1.006 (0.981–1.031)	0.991 (0.980–1.002)	0.986 (0.971–1.001)
lag 6	0.955 (0.872–1.047)	0.933 (0.827–1.052)	0.988 (0.913–1.069)	1.012 (0.988–1.037)	0.991 (0.981–1.003)	0.990 (0.974–1.006)
lag 7	0.936 (0.846–1.037)	0.936 (0.825–1.063)	0.951 (0.874–1.035)	0.985 (0.954–1.017)	0.976 (0.960–0.993)*	0.992 (0.977–1.007)
Stroke						
lag 0	1.016 (0.964–1.070)	1.030 (0.966–1.098)	1.049 (1.019–1.081)*	1.003 (0.992–1.015)	0.997 (0.9931.002)	0.995 (0.988–1.002)
lag 1	1.030 (0.978–1.086)	1.050 (0.985–1.119)	1.010 (0.980–1.042)	0.993 (0.981–1.005)	0.994 (0.987–1.000)	0.999 (0.992–1.006)
lag 2	1.017 (0.965–1.072)	1.033 (0.969–1.101)	1.024 (0.994–1.055)	0.996 (0.984–1.007)	0.997 (0.992–1.001)	1.001 (0.994–1.008)
lag 3	1.026 (0.975–1.081)	1.050 (0.986–1.118)	0.968 (0.935–1.001)	0.993 (0.982–1.004)	0.998 (0.994–1.002)	0.998 (0.991–1.005)
lag 4	1.026 (0.974–1.081)	1.039 (0.974–1.107)	0.984 (0.954–1.015)	0.992 (0.981–1.003)	0.996 (0.992–1.001)	1.007 (1.000–1.014)
lag 5	1.020 (0.967–1.075)	1.043 (0.978–1.112)	1.012 (0.981–1.043)	0.989 (0.977–1.001)	0.996 (0.992–1.001)	1.004 (0.997–1.011)
lag 6	1.043 (0.991–1.099)	1.052 (0.987–1.122)	1.020 (0.997–1.045)	0.990 (0.980–1.001)	0.993 (0.987–1.000)	1.005 (0.998–1.011)
lag 7	1.006 (0.954–1.061)	1.005 (0.941–1.073)	1.043 (1.014–1.072)*	1.001 (0.990–1.012)	0.998 (0.992–1.005)	1.002 (0.995–1.009)

Data are adjusted RR (95% CI). RR, relative risk; *, statistical significance level <0.05.

(3.5% per 10 µg/m^3 at lag day 6, relative risk =1.035, 95% CI: 1.002–1.070) (*Table 3*). Most probably the hospitalized patients were more vulnerable to the detrimental effect of air pollutants than community dwellers as they were more seriously ill and remained exposed to the ambient air pollutants in the open-air wards.

The daily mortality of community dwellers was sharply increased on lag days 0 and 2 of increased O_3 concentration (0.6% and 0.7%), whereas the relative risks of PM_{10}, $PM_{2.5}$, and NO_2 were 3%, 3.5–4%, and 0.8–0.9%, respectively and more delayed (lag day 6–7 for PM_{10} and $PM_{2.5}$ and lag day 4, 6 for NO_2, respectively) than that of O_3. The short-term lag patterns of the associations between air pollutant exposures and mortality were mainly limited to early days of exposure (lag 0–7 days) which is consistent with a previous report of air pollution-mortality relationship in Thailand (23). As in previous studies, non-accidental mortality increased after increase of level of O_3 value (23,25,26) and NO_2 (21). Interestingly, the associations between non-accidental mortality of PM_{10} and $PM_{2.5}$ in our study were increased (range, 3.00–4.00%, lag day 6–7) 3–10 times higher than that of previous studies (range, 0.28–1.10% and 0.22–0.71% for $PM_{2.5}$ and PM_{10}, respectively) (21-24). A meta-analysis of Asian studies indicated a mean increase in risk of 0.4–0.5% with a one-day per 10 µg/m^3 change in PM_{10} (23). It was reported that the likelihood of an adverse response to an inhaled pollutant depends on the degree of exposure and individual characteristics such as the susceptibility of the exposed person (29). Although, the individual susceptibility could not be identified with our study design, several factors could explain the higher mortality in our study. First, our study population group was elderly people of low socioeconomic status, with exposure to seasonal air pollution for several years due to their occupation, living and housing styles. The intensity [PM_{10} and $PM_{2.5}$ mean = 88.86 (40.25–208.63) and 61.76 (25.04–14.00) µg/m^3, respectively] and duration of exposure (3 months from February – April) of seasonal air pollutants during the study period could also significantly contributed to such a high mortality (*Figure 1*).

Our results for the two acute serious respiratory events, CAP and AECOPD, were consistent with the previous finding linking the lag structure between pollutant levels and emergency or hospitalization visits. The association between emergency visits for CAP was positive on the same day of increased pollutant levels and lag days from 1–4 days and 1–2 days for CO and O_3, respectively. Previous studies have reported that CAP increased shortly (lag day 0–5) after increased levels of SO_2, CO and O_3 (5,9). Although this study confirmed the association between gaseous air pollutants (SO_2, CO and O_3) and emergency visits for CAP, it did not confirm the association of any air pollutants with hospital admissions for CAP. The reason could be severe cases presenting to emergency room might be referred to the provincial hospital downtown or mild cases might be managed as outpatient cases. The association between emergency visits of AECOPD were positive at the same day of increased pollutant levels and lag day 1 for PM_{10}, whereas the lag period of $PM_{2.5}$ was at lag day 1 only which was consistent with some other studies (4,5). However, our previous report on the effect of PM_{10} on AECOPD in metropolitan area of Chiang Mai during seasonal smog was more delayed (lag day 7) (28). The difference of lag effect between the rural and urban area of the same province besides the difference in study years and degree of exposure to PM_{10} (e.g., housing style, occupation, protection awareness) might also be explained by the differences in disease severity and management (30). Emergency visits for AECOPD increased shortly (lag 1 day) after increased level of $PM_{2.5}$ (8,10) while, the association between hospital admissions for AECOPD was positive for both PM_{10} and $PM_{2.5}$ on lag day3 as shown in previous studies (4,6,11,31,32).

The association between air pollutants and emergency or hospitalization visits for cardiovascular events (MI and HF) were also demonstrated in our study. We found emergency visits, but not hospital admissions, of HF increased shortly after increase in O_3 concentration (lag day 4) as in the previous study (14). The likely reason could be the same as that for CAP. The previous reports also showed the similar results with our study that emergency visits for MI increased shortly after elevated level of NO_2 (ranged from lag day 0 and 2) (15,16). Emergency visits and hospital admissions for CVA increased after increase of level of SO_2 (ranged from Lag 0 and 6 day) as reported previously (17-19).

Enhanced oxidative stress and systemic inflammatory pathways triggered by free oxygen radicals from air pollutants capable of penetrating deep into alveoli was reported to play a key role in the pathophysiology of many pulmonary (33) and cardiovascular diseases (34,35) possibly increasing the rate of non-accidental mortality as in our study. The short-term lag pattern of the association between air pollution exposure and non-accidental mortality is very important for healthcare providers and public health authorities (23). Our results showing the impact of air pollution on non-accidental mortality was mainly limited to early days of exposure (lag day 0–7). Developing timely preventive measures are effective in reducing the health effects of air pollution is urgently required for extreme air pollution periods. Guo *et al.*, suggested that the government, public health and medical professionals, and general population should all be well aware of health warning systems and the perception of the dangers of air pollution (23).

The study has many strengths. Firstly, we use time series analysis to assess the trends and relationships using generalize linear models with Poisson regression analysis, which is in the same format as the previous studies (5,27,28). Secondly, the association between all air pollutants and health effects were adjusted with rain, pressure, wind speed, temperature, and humidity. Thirdly, we selected only Chiang Dao district population living in geographic areas exposed to the entire seasonal air pollution period as well as the whole day exposure with their open-air housing style, agricultural occupation, and the open-air wards of community hospital. Moreover, this community hospital is the only health facility that all local dwellers frequented to receive primary health evaluation and management.

Our study also has a number of limitations. Firstly, although the diagnoses of serious respiratory, cardiovascular, and cerebrovascular events were reviewed and adjudicated by dedicated team members and emergency room physicians, some relevant clinical data such as disease severity, clinical and biomedical risk factors, history of frequency of previous attacks, and management were not usually available in routine electronic medical records. However, these records were critically reviewed by the pulmonologist and cardiologist in the study team for relevant diagnoses. Secondly, the health care utilization and mortality data of only one hospital was chosen to estimate the impact of air pollutants, a possible selection bias could affect the validity of the results. However, data from only one hospital in the area could reflect the overall impact of the air pollutants for this specified area. Thirdly, there is no data about the association between long term exposure to air pollutions and health. Effect of long term air pollution should be addressed in the future studies. Lastly, this time series study was only conducted in one district (Chiang Dao district, Chiang Mai, Thailand). Therefore, these results can be generalized only to area s with the same pollution, environmental and socio-economic status.

Conclusions

Our study found that air pollutants are a major environmental health risk and effects on a variety of acute respiratory and cardiovascular diseases and increase non-accidental mortality. Thus, it is necessary to pay attention to the dangers of air pollution and to inform the public on how to minimize their risks from exposure to air pollution. Our findings support the government efforts in reducing high levels of air pollution, in order to improve the public health and reduce the burden of disease due to ambient air pollution in the population e.g., providing clean room, air purifier, and mask.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was approved by the Ethics Committee of the Faculty of Medicine, Chiang Mai University (Study code: MED-2558-03032, Date approval: 14th December 2015).

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