

Study on the Correlation between Temperature and Chronic Obstructive Pulmonary Disease in Shijiazhuang, China—Retrospective Cohort

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How to cite this paper: Fu, G.Q., Zhang, X.K. and Liu, H.Y. (2017) Study on the Correlation between Temperature and Chronic Obstructive Pulmonary Disease in Shijiazhuang, China—Retrospective Cohort. *Journal of Geoscience and Environment Protection*, 5, 23-31.

<https://doi.org/10.4236/gep.2017.57003>

Received: March 21, 2017

Accepted: July 8, 2017

Published: July 11, 2017

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Abstract

Using the chronic obstructive pulmonary disease (COPD) medical records from January 1st to December 31st of 2013 and the Meteorological observation data, the air pollution data in the same time periods, generalized additive models were used to quantitatively analyze the relationship between COPD hospitalizations and temperature with controlling the confounding effects of time trend, meteorological factors and air pollution index (AQI). Results showed: variable temperature in 24 h (BT), 3d lagged minimum temperature (Tm3) and 5d lagged diurnal maximum temperature and minimum temperature range (Tc5) have different effects on COPD hospitalizations. When BT is between -4.4°C and -0.7°C , the relative risk (RR) increases to 1.0207 (95% CI: 1.0074 - 1.0342) with every 1°C increase in BT; when Tm3 is between -3.6°C and 3.2°C , the relative risk (RR) increases to 1.0118 (95% CI: 1.0015 - 1.0222) with every 1°C increase in Tm3, and when Tm3 is greater than 20.5°C , the relative risk (RR) increases to 1.0069 (95% CI: 1.0005 - 1.0133) with every 1°C increase in Tm3; when Tc5 is between 0.9°C and 8.6°C , if the Tc5 increases 1°C , the relative risk (RR) increases to 1.0125 (95% CI: 1.0066 - 1.0185). There are different effects for weather in different seasons on COPD hospitalizations: in autumn and winter, it is mainly of little BT and heavy air pollution weather; in spring, the large Tc5 weather is a main feature, and in summer, it's mainly of high temperature and low pressure weather. The results help to provide some guidance on COPD forecasting services.

Keywords

Chronic Obstructive Pulmonary Disease (COPD), Temperature, Relative Risk (RR), Shijiazhuang

1. Introduction

Chronic obstructive pulmonary disease, or COPD for short, is a type of respiratory disease characterized by incompletely reversible airflow limitation as well as a common disease that seriously endangers people's health [1]. COPD is a major cause of disability, and it is the third leading cause of death in the United States. Currently, 16 million people are diagnosed with COPD. Many more people may have the disease and not even know it. COPD develops slowly. Symptoms often worsen over time and can limit your ability to do routine activities. Severe COPD may prevent you from doing even basic activities like walking, cooking, or taking care of yourself. At present, the etiology and pathogenesis underlying COPD are not fully elucidated, whereas it is certain that both meteorological and environmental conditions show a comprehensive effect on the incidence of COPD [2]-[7]. Yin Jun *et al.* [8] analyzed the difference in the incidence of COPD among different regions of China and the relationship between it and meteorological conditions, and they found that the incidence of COPD in North China was significantly higher than in South China.

North China is a region under frequent attack of both haze [9] [10] and respiratory diseases, whereas there are not many reports analyzing the effects of meteorological factors on COPD. In this study, we conducted a retrospective cohort study with the aim of studying the impact of air temperature on COPD and establishing prediction service indicators by means of using data of patients with COPD in some Grade A hospital from Hebei province and time series-based general additive model, thereby providing reference for public health meteorological service and scientific reference for public prevention from diseases and health fitness. COPD has no cure yet, and doctors do not know how to reverse the damage to the lungs. However, treatments and lifestyle changes can help you feel better, stay more active, and slow the progress of the disease.

2. Data Processing and Methods

2.1. Data and Processing

Data were selected from adults with COPD hospitalized in some Grade A hospital from Hebei province from January 1, 2013 to December 31, 2013. Data of patients who had been diagnosed by clinicians as COPD and who lived in Shijiazhuang were screened as the subjects.

The data included age, sex, region, duration of hospital stay, discharge time and doctors' diagnosis. The samples that met the criteria were subjected to duplicate checking according to name, age and hospitalization time, and a total of 984 samples were selected.

Meteorological data were provided by Hebei Meteorological Information Center, and the data of Shijiazhuang Station through ground observation from January 1, 2013 to December 31, 2013 were selected, including daily maximum temperature, minimum temperature, average temperature, average wind velocity, average relative humidity and average air pressure, etc.

Air pollution data mainly included daily air quality index (AQI) and PM_{2.5} concentration, which were provided by Hebei Provincial Environmental Protection Bureau.

As the impact of meteorological factors on diseases is continuous and cumulative, the cumulative effect of most influencing factors was larger than the impact of intraday effect on diseases [11]. Therefore, the intraday moving average and the first 1 - 6d moving average of the above-mentioned meteorological environment factors were derived as the basic factors and derived factors for analysis.

2.2. Research Methods

The number of patients with COPD was a small probability event in Shijiazhuang resident population, and its actual distribution was close to the Poisson distribution. In addition to the relationship with the number of hospitalized patients with COPD, air temperature and air pollution, it was also associated with the time factor, and the “holiday effect” might occur in the number of hospitalized patients with COPD. Therefore, when studying the impact of air temperature on COPD, other meteorological factors, atmospheric pollution and temporal trends as confounding factors should be correlated.

In the generalized additive model, a variety of nonparametric smoothing functions were used to control the confounding factors. It could adjust the long-term effects of time series and seasonal trends of changes, and eliminate the effect of holiday and other confounding factors [12] [13]. Therefore, we herein used the Poisson generalized additive model based on time series to establish the exposure-response relationship between the temperature and the number of hospitalized patients with COPD, which was achieved using Empower Stats analysis software [14].

3. Results

3.1. The Number of Hospitalized Patients with COPD and the Descriptive Characteristics of Main Meteorological Elements

A total of 984 hospitalized adults with COPD were admitted to some Grade A hospital in Shijiazhuang, Hebei Province from January 1, 2013 to December 31, 2013, including 56.4% males and 43.6% females, and the proportions of elderly patients over 60 years old and young and middle-aged patients were 51.2% and 48.8%, respectively.

Table 1 shows the number of inpatients with COPD in Shijiazhuang and the frequency distribution of meteorological elements. As shown in **Table 1**, the average number of inpatients with COPD in Shijiazhuang City in 2013 was 2.7/d, with the largest number being 9/d. The average temperature in Shijiazhuang in 2013 was 13.6°C, with the maximum and minimum temperature being 34.0°C and -8.1°C, respectively. This indicated that the annual average temperature was changed significantly. The temperature difference between day and night was large, with the average daily temperature difference and the maximum daily

Table 1. Statistical characteristics of COPD hospitalizations and meteorological, environmental factors in 2013.

	Mean	SD	Min	P25	Median	P75	Max
Hospitalizations	2.7	1.8	0	1.0	3.0	4.0	9.0
Average temperature/ $^{\circ}$ C	13.6	11.5	-8.1	3.4	14.2	24.1	34.0
Maximum temperature/ $^{\circ}$ C	18.1	12.0	-3.9	8.1	20.1	28.4	38.7
Minimum temperature/ $^{\circ}$ C	9.6	11.2	-12.3	-3.5	9.3	19.9	29.0
Day temperature change/ $^{\circ}$ C	-0.3	2.4	-9.8	-1.2	1.0	1.3	8.4
Daily temperature difference/ $^{\circ}$ C	8.5	3.5	0.9	6.2	8.4	10.7	21.5
Precipitation/mm	1.4	1.2	0.0	0.0	0.0	0.0	53.0
Relative humidity/%	60.7	20.2	13.0	46.0	60.0	77.0	99.0
Wind speed/(m/s)	1.9	0.8	0.3	1.4	1.8	2.3	6.4
Air pressure/hPa	1003.5	99.6	982.1	995.1	1004.3	1011.7	1030.0
AQI	219	125	50	129	180	269	500
PM _{2.5} /(μ g/m ³)	157.0	126.0	0	71.7	120.6	195.3	756.0

temperature difference being 8.5 $^{\circ}$ C and 21.5 $^{\circ}$ C, respectively. The daily temperature change was small, with the average daily temperature change, the maximum daily temperature decrease and the maximum daily temperature increase being -0.3 $^{\circ}$ C, 9.8 $^{\circ}$ C and 8.4 $^{\circ}$ C, respectively. The air pollution in Shijiazhuang in 2013 was heavy, with average AQI being 219, indicating heavy pollution. The data in **Table 1** were obtained from a top three hospitals in Hebei Province and the meteorological department of Shijia Zhuang.

3.2. Correlation of Meteorological Conditions with the Number of Hospitalized Patients with COPD

Maximum temperature (Tmax), minimum temperature (Tmin), mean temperature (T), daily temperature range (Tc), 24h average temperature change, rainfall (R), wind speed (F), relative humidity (T), air pressure (AP), air quality index (AQI), PM2.5 concentration and the moving average values of the above-mentioned factors lagging 1 - 6d were introduced into the model together with the time trend and Holiday so as to study the relationship between meteorological conditions and the number of inpatients with COPD. If the same factors lagging different days affected COPD, the factor with the strongest effect was selected and the others should be omitted. **Table 2** shows the P values of various factors affecting the number of patients with COPD and their degrees of freedom. As shown in **Table 2**, Tc5, BT, Tmin3, AP5, R, AQI, Time and Holiday all affected the number of patients with COPD. Time item is a time series, that is, the trend analysis of the time series. Holiday was a stratification variable, with Saturday,

Table 2. Correlation between COPD hospitalizations and meteorological, environmental factors.

	Tc5	BT	Tmin3	AP5	R	AQI	Time	Holiday
P. value	0.004**	0.007**	0.068*	0.015*	0.023*	0.012*	0.016*	0.004**
Degree of freedom	3.97	7.38	3.93	3.4	1	1	6.18	

Note: **P < 0.001, *P < 0.01.

Sunday and statutory holidays being 0 and non-holidays being 1, and the others were continuous variables. From the fitting degree of freedom, there was a linear relationship between AQI, R and the number of hospitalized patients with COPD, while there was a non-linear relationship between the other variables and the number of hospitalized patients with COPD. And in light of P. values, BT and Tc5 were the main meteorological factors influencing the onset and hospitalization of COPD.

3.3. Impact of Temperature Changes on the Number of Hospitalized Patients with COPD

The impact of temperature changes on the number of hospitalized patients with COPD was studied after the trend of time change and other meteorological factors had been controlled. **Table 3** shows the effect value and the relative risk (RR) (95% CI) of the changes in the number of inpatients with COPD for each change of 1°C in daily temperature range (Tc5), 24-hour temperature change (BT) and minimum temperature (Tmin3) in Shijiazhuang in 2013.

As shown in **Table 3**, when $Tc5 \leq 8.6^\circ\text{C}$, $\beta > 0$, and with the increase in Tc5, the number of inpatients with COPD tended to increase, indicating that when $0.9^\circ\text{C} < Tc5 \leq 8.6^\circ\text{C}$, with the increase in Tc5, RR of hospitalization of patients with COPD tended to increase ($RR > 1$). When $Tc5 > 8.6^\circ\text{C}$, $\beta < 0$ and $RR < 1$, indicating that with the increase in Tc5, the number of inpatients with COPD tended to decrease and that RR of hospitalization of patients with COPD tended to decrease. The impact of BT on the number of inpatients with COPD was changed with fluctuations. When BT was at -0.7°C , the number of patients was in a relative peak period, while when BT was at -4.4°C and 5.2°C , the number of patients was relatively small. $RR > 1$ and the risk of incidence and hospitalization of COPD were increased with the increase of temperature change when $-4.4^\circ\text{C} < BT \leq -0.7^\circ\text{C}$, and $RR < 1$ and the risk of incidence and hospitalization of COPD was decreased with the increase of temperature change when $-0.7^\circ\text{C} < BT \leq 5.2^\circ\text{C}$. When $BT \leq -4.4^\circ\text{C}$ and $BT > 5.2^\circ\text{C}$, P values were not statistically significant. As shown in the statistical data, when $BT \leq -4.4^\circ\text{C}$ and $BT > 5.2^\circ\text{C}$, the annual number of samples was only 18, which appeared mainly under the influence of the significant cold air in winter and spring and of the fumigation effect in spring. Similarly, when $Tm3 \leq -3.6^\circ\text{C}$ and $3.2^\circ\text{C} < Tm3 \leq 20.5^\circ\text{C}$, the corresponding $RR < 1$, indicating that the minimum temperature lagging 3 days was in this range. With the increase in Tm3, the risk of incidence and hospitalization of

Table 3. Relative risk of COPD hospitalizations, while different air temperature indicates.

	Index value	β	RR	95% CI	P
Tc5	≤ 8.6	0.01247	1.0125	1.0066 - 1.0185	<0.0001
	> 8.6	-0.00906	0.9910	0.9852 - 0.9968	<0.0024
	≤ -4.4	-0.0007	0.9993	0.9834 - 1.0154	<0.9310
BT	-4.4 - -0.7	0.0205	1.0207	1.0074 - 1.0342	<0.0022
	-0.7 - 5.2	-0.00837	0.9917	0.9869 - 0.9964	<0.0006
	> 5.2	0.01394	1.0140	0.9819 - 1.0473	<0.3967
Tmin3	≤ -3.6	-0.00899	0.9986	0.9825 - 0.9996	<0.0405
	-3.6 - 3.2	0.01174	1.0118	1.0015 - 1.0222	<0.0244
	3.2 - 20.5	-0.00144	0.9917	0.9839 - 0.9996	<0.0384
	> 20.5	0.00689	1.0069	1.0005 - 1.0133	<0.0332

COPD showed a decreasing trend. While when $-3.6^{\circ}\text{C} < \text{Tm}3 \leq 3.2^{\circ}\text{C}$ and $\text{Tm}3 > 20.5^{\circ}\text{C}$, $\text{RR} > 1$, indicating that with the increase in $\text{Tm}3$, the risk of incidence of COPD was increased and the number of inpatients was increased.

Therefore, when $0.9^{\circ}\text{C} < \text{Tc}5 \leq 8.6^{\circ}\text{C}$, $-4.4^{\circ}\text{C} < \text{BT} \leq -0.7^{\circ}\text{C}$, $-3.6^{\circ}\text{C} < \text{Tm}3 \leq 3.2^{\circ}\text{C}$ and $\text{Tm}3 > 20.5^{\circ}\text{C}$, for every elevation of 1°C in $\text{Tc}5$, BT and $\text{Tm}3$ in their respective range, RRs of incidence and hospitalization of COPD were (95% CI: 1.0066 - 1.0185), 1.0207 (95% CI: 1.0074 - 1.0342), 1.0118 (95% CI: 1.0015 - 1.0222) and 1.0069 (95% CI: 1.0005 to 1.0133), respectively. In general, the temperature is an important factor in hospitalization of chronic obstructive pulmonary disease in residents.

3.4. Discussion of the Impact of Air Temperature on COPD

On the basis of the above analysis, we further analyzed the daily average temperature change as the weather inducer affecting the incidence and hospitalization of COPD in Shijiazhuang. As for Shijiazhuang, generally speaking, $|\text{BT}| < 3^{\circ}\text{C}$ indicated the lack of impact of cold air and that the atmosphere was relatively stable, $3^{\circ}\text{C} \leq |\text{BT}| < 6^{\circ}\text{C}$ indicated a weak impact of cold and warm air, and $|\text{BT}| \geq 6^{\circ}\text{C}$ indicated a significant impact of cold and warm air. According to the threshold of BT , BT in the vicinity of -0.7°C was the relative peak of the incidence and hospitalization of COPD, and BT in the vicinity of -4.4°C and 5.2°C was the relative nadir of the incidence and hospitalization of COPD. By combining the daily meteorological forecast service, we sequenced all the data according to the change of BT , and we found a total of 308 samples in the relative incidence peak of COPD. Statistical analysis of the corresponding weather characteristics showed that when temperature was little changed in autumn and winter, AQIs at the corresponding time were both very large, with the average values being 337 (serious pollution) in winter and 211 (heavy pollution) in autumn, both reaching the heavy pollution and above. When $|\text{BT}| < 3^{\circ}\text{C}$ in autumn and winter, the number of days with severe pollution and moderate pollution accounted for 62.5% and 73.2%, respectively. The above analysis showed that AQI and the number of hospitalized patients with COPD were related to each

other. Therefore, autumn and winter, weather stability in time of small temperature changes, and air pollution represented the major factors for COPD. The study by Fu Guiqin *et al.* showed that the atmosphere in autumn and winter in Shijiazhuang was stable, which was not conducive to the proliferation of pollutants and gave rise to weather pollution easily. The conclusion of the study by Zhang *et al.* also confirmed the impact of air pollution on respiratory diseases.

The characteristics of the weather influence in spring are as follows: the weather in spring gets warmer, the temperature difference is increased, and the average daily temperature difference is 10.0°C. It is cold in the morning and hot at noon, which leads to cold easily. The study by Zhang *et al.* [9] showed that the activity of bacteria in spring began to enhance and populations with weak immunity were vulnerable to cold, which was one of the main reasons for the incidence of COPD. Statistics of the lowest temperature in Shijiazhuang from 1981 to 2010 showed that the lowest temperature of 3.2°C mainly occurred in middle and late March and late November. During seasonal transformation period, the temperature changes were an inducer for the incidence of COPD.

It is hot in summer, and the temperature during the day and night is very high. The average minimum temperature reaches 23°C and the average pressure stands at 991.7 hPa. High temperature and low pressure make people feel hot and stuffy easily, and they will feel tired when they sleep poorly at night, which results in decreased immunity and disease recurrence. Therefore, the impacts of meteorological factors in different seasons on COPD are different. So the impact of temperature on the number of hospitalized patients with COPD not only shows the characteristics of weather process, the impact of seasonal changes is more significant.

4. Conclusion and Discussion

1) The temperature changes significantly within the year in Shijiazhuang; the temperature difference between day and night is large; the daily temperature changes are small; and the air pollution is heavy. The temperature change is a main meteorological factor influencing the incidence of COPD in adults in Shijiazhuang.

2) After such confounding factors as time trend, other meteorological factors and atmospheric AQI had been controlled, we found that BT, Tm3 Tc5 as the indicators of the threshold of the number of hospitalized patients and the impact characteristics: when $-4.4^{\circ}\text{C} < \text{BT} \leq -0.7^{\circ}\text{C}$, $-3.6^{\circ}\text{C} < \text{Tm3} \leq 3.2^{\circ}\text{C}$ and $\text{Tm3} > 20.5^{\circ}\text{C}$, $0.9^{\circ}\text{C} < \text{Tc5} \leq 8.6^{\circ}\text{C}$, for each increase of 1°C in BT, Tm3 and Tc5, RRs of incidence of COPD were 1.0207 (95% CI: 1.0074 - 1.0342), 1.0118 (95% CI: 1.0015 - 1.0222), 1.0069 (95% CI: 1.0005 - 1.0133) and 1.0125 (95% CI: 1.0066 - 1.0185), respectively.

3) When the 24 h temperature change was small in Shijiazhuang ($\text{BT} = -0.7^{\circ}\text{C}$), the number of hospitalized patients with COPD was relatively large. When $|\text{BT}| < 3^{\circ}\text{C}$, the seasonal change characteristics of the number of hospitalized patients with COPD affected by weather were that fall and winter seasons

were mainly associated with air pollution in stable weather; that spring was associated with the impact of large temperature difference, and that summer was associated with high temperature, low pressure and hot weather.

4) The factor of meteorological environment is only one aspect affecting the incidence of COPD, and the incidence and hospitalization are also associated with such factors as their own habits and physical characteristics. In addition, the data of COPD in this study were limited, and continued attention to the study is needed.

Most of the time, COPD is diagnosed in middle-aged or older adults. The disease is not contagious, meaning it cannot be passed from person to person.

COPD has no cure yet, and doctors do not know how to reverse the damage to the lungs. However, treatments and lifestyle changes can help you feel better, stay more active, and slow the progress of the disease.

Acknowledgements

The study was jointly funded by the Hebei Meteorological Bureau for the fund project (14KY12) and the Provincial Department of Finance Haze Research (HB2015073610030001).

References

- [1] Bai, J.A., Zhao, J., Shen, K.L., *et al.* (2010) Current Trends of the Prevalence of Childhood Asthma in Three Chinese Cities: A Multicenter Epidemiological Survey. *Biomedical and Environmental Sciences*, **23**, 453-457.
[https://doi.org/10.1016/S0895-3988\(11\)60007-X](https://doi.org/10.1016/S0895-3988(11)60007-X)
- [2] Tao, Y., Yang, D.R., Lan, G., *et al.* (2013) Relationship between Air Pollutant and Respiratory Disease Hospitalization an Lanzhou. *China Environmental Science*, **33**, 175-180.
- [3] Yue, H.Y. and Shen, S.H. (2009) Advance in the Relationship between Respiratory and Card Io-Cerebrova Scular Diseases and Meteorological Conditions. *Journal of Meteorology and Environment*, **25**, 57-61.
- [4] Wang, M.Z., Zheng, S., Wang, S.G., *et al.* (2012) A Time-Series Study on the Relationship between Gaseous Air Pollutants and Daily Hospitalization of Respiratory Disease in Lanzhou City. *Health Research*, **41**, 771-775.
- [5] Li, Q.M., Zhou, X.Z., He, X.J., *et al.* (1991) Relationship between Chronic Obstructive Pulmonary Disease (COPD) and Meteorological Factors. *Journal of Jinzhou Medical Coilege*, **12**, 306-307.
- [6] Zhang, S.Y., Zhang, X.K., Xie, J.F., *et al.* (2012) Analysis of Relationship between Colds and Weather Conditions and the Establishment of Medical Forecast in Baishan City. *Meteorological Monthly*, **38**, 740-744.
- [7] Zeng, Y.H., Guo, L.P., Zhang, Y., *et al.* (2003) Relationship between Hospitalization and Climatic Factors in Patients with Chronic Obstructive Pulmonary Disease (COPD). *Gaungzhou Medical Journal*, **24**, 123-132.
- [8] Yin, J., Tan, J.G., Zhu, L.M., *et al.* (2007) Correlation Analysis between Chronic Obstructive Pulmonary Disease and Meteorology Factors in Different Areas. *Meteorological Science and Technology*, **35**, 841-844.
- [9] Fu, G.Q., Zhang, Y.X., Gu, Y.L., *et al.* (2014) Change of Haze Day and Its Forming

Reason in Hebei Province. *Journal of Meteorology and Environment*, **30**, 51-56.

- [10] Fu, G.Q., Zhang, X.M., You, F.C., *et al.* (2016) Effect of Meteorological Conditions on PM_{2.5} Concentration in Shijiazhuang of Hebei. *Journal of Arid Meteorology*, **34**, 349-355.
- [11] Wang, M.Z., Zheng, S., Wang, S.G., *et al.* (2012) Time-Series Analysis of the Number of Air Pollutants and Respiratory Diseases on the Day of Hospitalization in Lanzhou City. *Journal of Hygiene Research*, **41**, 771-775.
- [12] Jiang, Y.F., Wang, L.P., Yi, L., *et al.* (2015) Relationship between Daily Temperature and Emergency Department Visits for Abdominal Pain in Beijing City. *Journal of Lanzhou University (Natural Sciences)*, **51**, 103-108.
- [13] Wu, F., Jing, Y.S., Li, X.Y., *et al.* (2013) Application of Generalized Additive Model in Research of Influence of High Temperature and Heat Wave on Human Health. *Science Technology and Engineering*, **13**, 5915-5919.
- [14] Cen, C.Z., Chen, X.L. and Wei, C. (2016) *Epidemiological Data Analysis and Empower Stats Software Application*. Shanghai Scientific & Technical Publishers, Shanghai.



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