Relationship of Air Pollution and Daily Hospital Admissions Due to Respiratory Disease: A Time Series Analysis

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A R T I C L E   I N F O

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ABSTRACT

Introduction: Air pollutants and respiratory diseases have a significant relationship and cause major health problems. Low attention has been paid to the daily hospital admissions due to the presence of pollutants in desert cities such as Yazd city, Iran. Therefore, this study aimed to investigate the short-term relationship between air pollution and daily hospital admissions due to respiratory disease in Yazd hospitals.

Materials and Methods: This cross-sectional study investigated pollutants including PM_{10}, CO, SO_2, NO_2, and O_3 recorded daily in Yazd air pollution monitoring station. Moreover, the daily hospital admissions (sample size =180) of the pulmonary patients were collected from government hospitals from March to September 2017.

Results: The results showed that PM_{10} concentrations were higher than the Environmental Protection Agency (EPA) and World Health Organization standards. Furthermore, only 7.6% of the patients' diseases were attributed to air pollution. The highest correlation (R = 0.595 and P = 0.002) was observed between daily hospital admissions and NO_2 concentration. However, after age adjustment in regression analysis, this relationship was also significant for O_3. The behavior and variations of pollutants were interpreted by time series using auto-regressive moving average (ARMA) (1,1). The results showed that the best correlation was found between pollutants and admission of the patients at lag = 48 hr.

Conclusion: The daily admission of patients to hospital due to pulmonary disease was highly related to NO_2 and O_3. However, the correlation of admission with CO, PM_{10}, and SO_2 was not significant, because NO_2 and O_3 are oxidation factors and stimulate the respiratory system.

Introduction

Air pollution is an important environmental issue due to its serious impacts on human health. Air pollutants such as CO, NO_2, SO_2, O_3, and PM are mainly emitted from fossil fuels' combustion [1].

According to the World Health Organization (WHO), approximately 3.5 million deaths occur due to air pollution annually. Many air pollutants such as CO, NO_2, SO_2, O_3, particulate matter (PM_{10}), heavy metals, radon, etc. have negative

health effects [2]. This rate increased by 60% from the year 2000 to 2010 and 65% of the deaths were attributed to the Asian countries [3]. In the recent two decades, epidemiological studies showed that air pollution caused cardiovascular and respiratory problems, lung function defect, chronic bronchitis, and death [4]. Moreover, lack of birth weight, pulmonary disorders, acute heart attacks, cardiovascular diseases, and other illnesses were related to urban air pollution [5]. Among these diseases, outbreak of pulmonary diseases and daily hospital admissions due to respiratory disease were among the most significant indicator diseases associated with air pollution. In this regard, epidemiological and laboratorial observations proved specific roles of the suspended particles, O_3, NO_2, and SO_2 on human health [6]. These factors have a significant role in stimulation of the respiratory system, oxidation, reduction in the lung capacity, and lung cell immunity against biological factors. As a result, a variety of diseases raise in the respiratory tract, which may lead to death [7]. The consequent increased rate of hospital admission can lead to an additional burden on the health system. Similar studies in other cities of Iran showed that environmental pollutants affected the mortality rate and pulmonary diseases with an increasing trend in urban areas [8]. Some studies investigated the relationship between air pollution and the number of patients admitted to hospitals, but this relationship has not been determined in Yazd city. Epidemiological and human studies confirmed the relationship between air pollutants and types of diseases [7,9,10]. As a result, the authorities are recommended to try to reduce the disease burden related to air pollution. Yazd is located in the central desert regions of Iran, where the amount of suspended particles has increased with increase of desertification trend and dust streams. So, the quality of air is highly affected in this region by natural phenomena such as dust stream[11]. The current study aimed to investigate the correlation between air pollution and respiratory disease by using time-series analysis in Yazd city, but according to similar studies did

not investigate the confounder factors [10,12-14]. However, statistical models are among the effective methods in health studies caused by air pollution. Nevertheless, statistical models such as regression can adjust the confounders; time series models can determine the trend, behavior, and time variations of the parameters. Other benefits of time series include modeling and forecasting of variation trend based on the past data. Considering the effect of air pollution, especially suspended particles, on outbreak of the respiratory diseases and the gap in the relationship between these two factors [13], this study was conducted. Moreover, variation trend of the air pollution and daily admission hospital rate were determined.

Materials and Method

Location study

Iran is a high plateau located at latitudes within the range of 25- 40° in an arid zone in the northern hemisphere of the Earth. The world's most oppressive deserts are located in center of the large and closed cradle of Iran's plateau, at the center of Yazd province, which is surrounded by large deserts, such as Loot and Dashte Kavir [15].

Air pollution and health data

Daily average concentrations of the five significant pollutants (SO_2 ،NO_2،O_3،CO،PM_{10}), were taken from two monitoring air pollutants stations of Yazd Environmental Protection Agency in 2017 (March 25 to September 22, 2017). All five pollutants was precisely monitored at both stations during one year and full information of the indicator pollutants was collected and analyzed by a time series method. Information about the daily hospital admission due to pulmonary diseases was collected from Shahid Sadoughi Hospital and Shahid Rahnemoon Hospital of Yazd. These two hospitals were selected since they are among the largest public hospitals of Yazd and most of the emergency patients refer to them. Considering that the studied respiratory patients referred to these centers less frequently due to air pollution, the total number of pulmonary diseases were classified monthly.

Statistical analyses

Descriptive statistics (including mean, frequency, minimum, maximum, percent, and Standard) and chi-square test were run to analyze the epidemiological data. The data trend of time variation (the daily admission of patients versus the concentration of pollutants) was investigated and modeled within the studied time by time series using autoregression moving average (ARMA). Autocorrelation Function (ACF) and partial autocorrelation functions (PACF) are two suitable tools for determining the primary q (the order of the MA part) and p (order of AR part), respectively. The Root mean square error (RMSE) criterion derived from fitting of the model and the Box-Pierce test were used to determine the best model. Accordingly, AR and ARMA models were checked with different parameters and the suitable models were selected. Among the selected models, the model with lower RMSE was selected as the best model. The RMSE ranged from 3.82 to 10.81 (3.72, 3.8, 10.24, and 10.81); therefore, ARMA (1,1) was selected as best model. The lags between the daily admitted patients due to pulmonary disease and the concentration of air pollutants in =12, 24, 36, 48 hr. were evaluated using this model. In this study, the Poisson regression model was used to describe and predict the average daily admission of patients with pulmonary diseases. The Pearson correlation statistic (r) was also applied to determine the significant relationship between air pollutants and the daily admission of patients due to pulmonary disease. Moreover, regression analysis was used to describe the average parameters. Time series modeling using $Minitab_{17.1}$, Poisson regression analysis using $Stata_{14.2}$, and correlation test were run using $SPSS_{20}$. The significance level was less than 0.05.

Ethical issues

This study was conducted with approval of Shahid Sadoughi University of Medical Sciences and Health Services, Medical Ethics Committee. Code: IR. SSU. SPH.REC.1397.164.

Results

The average daily admission of patients due to pulmonary diseases was 9.7%, with an average age of 34.5. This study aimed to investigate the relationship between air pollution and daily hospital admissions due to respiratory disease using the time series model.

In this study, the average Air Quality Index (AQI) [16] was in a good state, only PM_{10} was at a moderate level. The suspended particle concentration was in this range (in a good state, according to AQI index) during 96% of days. Moreover, the suspended particles' concentrations were unhealthy for sensitive, unhealthy, and at-risk individuals in 10%, 2%, and 1.6% of the total days, respectively.

The relationship between other pollutants and daily admission patients was insignificant (P > 0.05).

On the contrary, exposure to PM_{10} was associated with death and cardio-respiratory diseases. However, lags (3 days) were observed between the PM concentration and its health effect.

Regression analysis

Since a disease outbreak depends on the interaction between several mechanisms and factors, regression analysis was used to determine the relationship between variables and their effects on each other [14]. Regarding the specific accountability of the responses, Multiple Poison Regression was used (Table 1). In this study, the daily admission of the patients to hospital was considered as a dependent variable and the pollutants' concentration as an independent variable.

Table 1: Regression analysis of the associated factors with hospital referring

Response	Unit	IRR	SE	T-value	P-value	95% conf. Interval	
O_3	$\mu g/m^3$	0.986	0.0067	-1.97	0.049	0.97	0.99
PM_{10}	$\mu g/m^3$	1	0.00023	0.56	0.573	0.99	1
NO_2	$\mu g/m^3$	0.999	0.00024	-1.1	0.271	0.99	1
Average		0.98	0.0018	-8.87	0.000	0.97	0.98
Constant		23.05	3.8	18.97	0.000	16.67	31.88

Age is one of the confounders adjusted in our regression models. According to the regression model, the relationship between O_3 and the daily admission of patients to hospital due to pulmonary diseases was statistically significant (p < 0.049). In other words, 1 unit of increase in O_3 concentration increases the risk of pulmonary diseases about 0.986. Variations of patients' daily admission to the hospital versus O_3 concentrations are shown in Figure 1.

$$y = -0.6857x + 24.443$$
$$R^2 = 0.1275$$
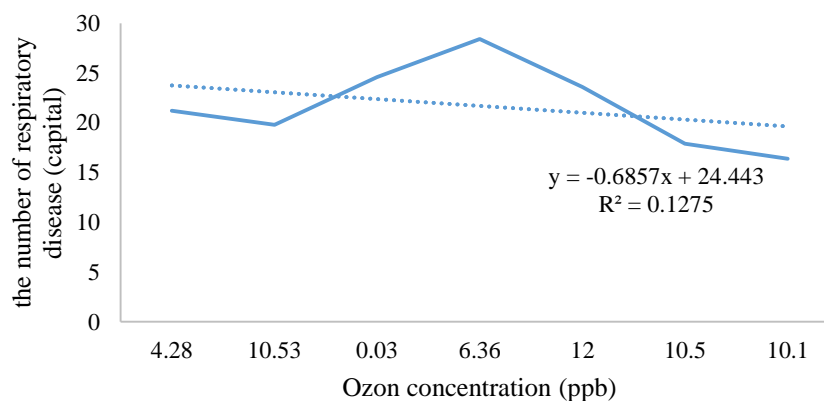
Figure 1: The number of patients' variations in different concentrations of O_3

Although O_3 acts as an oxidation agent for membrane receptors, intracellular kinases and phosphatases, and transcription factors, as inflammation regulator in the body [17]. Based on the findings, $r^2 = 0.076$ means that only 7.6% of the daily admitted patients could be explained by concentration of O_3 in the atmospheric air.

Time series

Time series models are one of the most suitable studies in the field of short-term effects of air pollution on health [12]. In the current study, the hospital admission rate for respiratory disease was considered as a health indicator. Even though studying the effect of air pollution on daily admission of patients to hospital can only investigate a small proportion of the population [18]. However, process and variations of variables over time are done using time series. Investigated models for smoothing the confounding agent included AR and ARMA, which analyzed p and q 1-5. According to the results, AR (3), AR (4), ARMA (1, 1), and ARMA (3,3) were statistically significant and their details are given in Table 2.

Table 2: Time series models for consideration of hospital visits

AR(4)	Coef	SE(coef)	P-value	-
Constant	0.5351	0.2698	0.049	-
Mean	10.81	5.451		-
AR(1)	0.29	0.074	0.013	-
AR(2)	0.1882	0.0748	0.013	-
AR(3)	0.2726	0.0752	0.000	-
AR(4)	0.1996	0.2698	0.049	
Modified Box-pierce test	Lag	Chi-square	Df	P-value
-	12	25.2	7	0.001
-	24	38.1	19	0.006
-	36	47.3	31	0.031
-	48	60.4	43	0.041
AR(3)	Coef	SE(coef)	P-value	-
Constant	1.0094	0.2637	0.000	-
Mean	10.24	2.676		-
AR(1)	0.3498	0.0712	0.003	-
AR(2)	0.2231	0.0746	0.000	-
AR(3)	0.3285	0.0727	0.000	-
Modified Box-pierce test	Lag	Chi-square	Df	P-value
-	12	26.7	8	0.001
-	24	39.3	20	0.006
-	36	48.8	32	0.029
-	48	62.4	44	0.035
ARMA(3,3)	Coef	SE(coef)	P-value	-
Constant	-0.154	-0.11	0.179	-
Mean	3.807	2.82	0.000	-
AR(1)	-0.7188	0.0535	0.000	-
AR(2)	0.86	0.0424	0.000	-
AR(3)	0.89	0.0586	0.000	-
MA(1)	-0.8998	0.0549	0.000	-
MA(2)	0.7546	0.0698	0.000	-
MA(3)	0.9193	0.0243	0.000	-
Modified Box-pierce test	Lag	Chi-square	Df	P-value
-	12	10.7	5	0.058
-	24	20.7	17	0.239
-	36	31.2	29	0.357
-	48	39.8	41	0.523
ARMA(1,1)	Coef	SE(coef)	P-value	-
Constant	-0.042	-0.028	0.000	-
Mean	3.73	2.497	-	-
AR(1)	-0.04	-0.028	0.138	-
MA(1)	1.011	0.004	0.000	-
-	0.94	0.0287	0.000	-
Modified Box-pierce test	Lag	Chi-square	Df	P-value
-	12	14.7	9	0.099
-	24	26.7	21	0.18
-	36	36.9	33	0.292
-	48	46.1	45	0.425

According to Table 2, the ARMA (1, 1) model was the best model for explaining the effect of air pollution on daily admission of patients to hospital due to respiratory disease, because its mean was less than the other models. Furthermore, these models are suitable for shock-induced systems such as the daily admission patient to hospital due to pulmonary disease. AR (3) and AR (4) models were statistically significant (p < 0.001), but their coefficient was not statistically significant.

In this study, time series' models were also evaluated in lag = 12, 24, 36, and 48. Results showed that exposure to air pollutants during 48 hours (lag = 4) was the most effective agent on the daily admission of patients to hospital due to pulmonary disease in Yazd. However, the statistical difference was significant in the modified Box-pierce for AR (3) and AR (4)

models. According to Table 2, with increase of lags, chi-square and P increased in ARMA models ($P < 0.02$) considering the delay in admission of patients to hospital due to respiratory diseases. With regard to the results, ARMA (1, 1) was selected as the best model and trend of the predicted variation based on this model was shown by the residual plots (Figure 2).
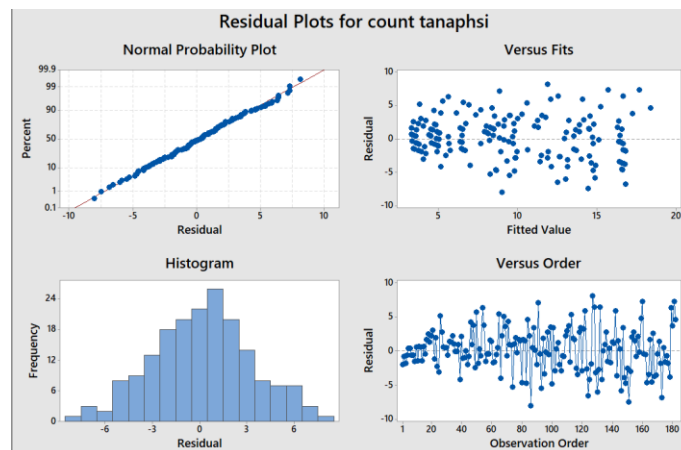
Figure 2: Histogram plots of residual, residual versus fitted values, residual versus ordered times, and normal probability for hospital visit in fitting ARMA

As shown in figure 2, the fitting was perfectly suitable and aptness of the proposed model was confirmed. Adequacy data also showed that autocorrelation and partial autocorrelation were near to zero, which showed insignificancy of the residuals in all lags. In the following, the plot of observed versus fitted data during the study period is shown in figure 3.

According to Figure 3 and 4 difference between the fitted and observed values is low. However,

due to the study short duration, the frequency of variation was not determined in time series. Considering the important effect of air pollutants on outbreak of the respiratory diseases and the depended-variations' trend of admission patient to hospital with air pollution, further investigations are required at higher periods. This relationship can be investigated regarding other diseases such as cardiovascular diseases.
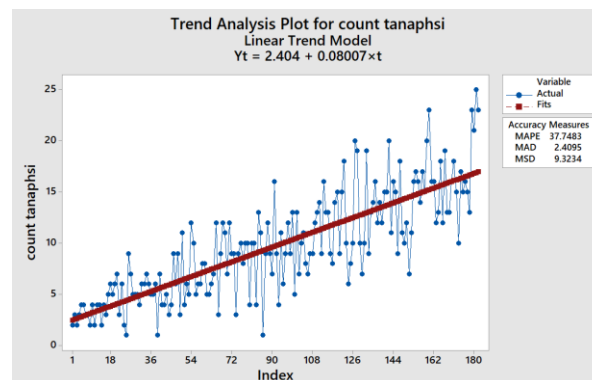

Figure 3: Average plots of the observed and fitted values for hospital visits using ARMA (1.1)
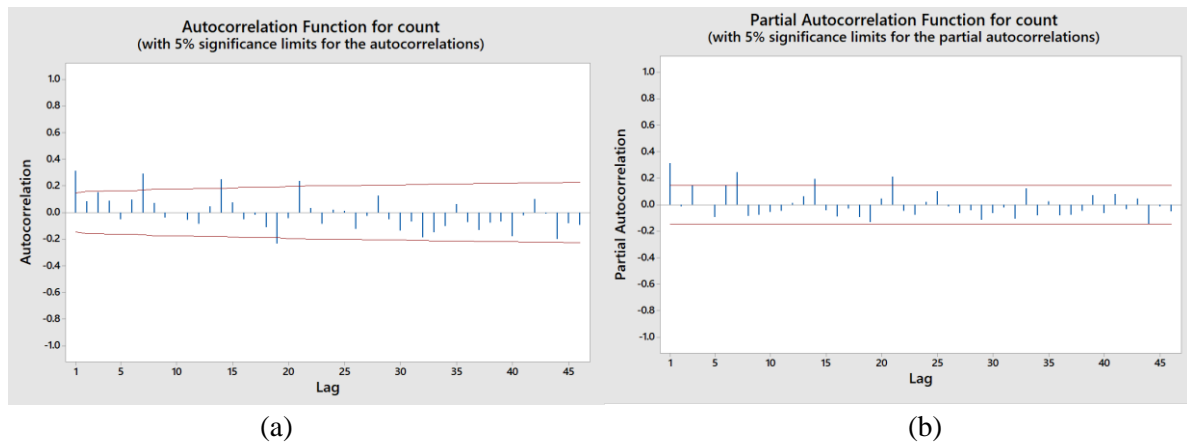
Figure 4: ACF Plot (a) and PACF Plot (b)

Discussion

A total of 1770 patients were admitted in the studied hospitals due to respiratory diseases in Yazd. Among the patients, 808 were women and were 962 men. Only the annual average of PM_{10} exceeded from the WHO standard [19], while the other factors were within the acceptable range. High concentration of PM was observed in many Asian cities due to the specific properties of this geographic reign [20]. According to the meteorological data, Yazd City is located in the warm and dry area of Iran in a desert region, where many local and regional dust steams occur. The correlation between CO and SO_2 was more than the other factors ($r^2 = 0.145$, $p < 0.05$), because they are the primary contaminants emitted to air from combustion of fuel. Therefore, their correlation can be due to similarity of the emission source and the effective environmental conditions that involve these pollutants in the atmosphere [21]. Recently, many studies have been conducted on potential mechanisms of the exposure to air pollutants that lead to respiratory disease. For example, air pollutants can cause damage to epithelial cells and macrophages, which may reduce the body's defense mechanisms against pulmonary infections or increase the reactivity of respiratory system cells. The severity of cell damages varied according to the concentration of contaminants, exposure duration, and type of pollutant. However, our results showed a significant and positive correlation between air pollution and prevalence of respiratory diseases [22].

So, the outbreak of pulmonary illnesses, mortality rate, and admission of patient to hospital increased noticeably [18]. In the current study, was tried to determine the correlation between air pollution in Yazd city and daily admission of the patient to hospital due to pulmonary diseases using the Pearson test. The findings indicated that health effects of air pollution on human health can be observed as the rate of patients' daily admission to hospital.

The correlation between CO and SO_2 was more than other factors ($r^2 = 0.145$, $p < 0.05$). Results showed that the correlation between daily admission of patients to hospital and the concentration of NO_2 was higher than other pollutants ($r^2 = 0.4$) ($p < 0.001$), because NO_2 stimulated the pulmonary system in higher depth. Moreover, the secondary particulate matters, such as PANs are generated due to the influence of NO_2 on allergic reactions and acute disease [23,24]. In other studies, the 4% NO_2 increased acute respiratory infections[22]. Moreover, toxicological evidence showed that NO_2 had an indirect effect on the pulmonary illnesses and infections, because it may increase the sensitivity of respiratory cell to bacterial and viral infections [25]. Moreover, this correlation between pulmonary illnesses and NO_2 may be due to the photolysis process of the No_x cycle. This is due to the fact that NO is emitted from the moving resources as primary pollutant and is involved in atmospheric reactions related to light. This reaction was improved in hot and dry

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climate such as Yazd. On the other hand, presence of a high level of humidity can limit it [26]. Moreover, the correlation between patients' admission and CO and PM_{10} was negative (p < 0.05) since the health effect and toxicity of CO are related to indoor space and climatic pattern that generated COHb and reduced the transportation capacity of oxygen in the blood [27]. Therefore, CO is not related to the mortality rate and hospital admission due to the pulmonary disease. PM_{10} can penetrate into the human pulmonary system and create inflammatory and allergenic responses. Moreover, various chemical and microbial contaminants aggregated on its surface, which cause synergistic effects [25].

Considering that these pollutants do not have protective effects on the health, application of models able to determine the co-effects and the variation trend during time is necessary [13,14].

About 92% of the diseases are multifactorial and depend on many factors, such as socio-economic, genetic, and other factors. Moreover, modeling and determining the trend of changes during the period of study were used by time-series models with regard to the synergistic effects of contaminants on creating health complications.

A significant difference was found between the observed and fitted values, which indicates inappropriateness of used models in this study. On the other hand, P in ARMA grade 1 and 3 was statistically significant, indicating that the model was suitable.

With regard to the delayed effects of air pollution on health, identification of the health risks is significantly necessary. However, the findings are controversial regarding the effect of lags on the relationship between air pollutants and health effects [10].

Conclusion

In this study, the relationship between air pollution and the number of pulmonary patients in Yazd was studied.

- The air quality index for Yazd was good; because the average concentration of air pollutants was less than the EPA and WHO standards (except

PM_{10} that exceeded from this limit during 4% of the study days).

- The daily admission of patients to hospital due to pulmonary disease was highly correlated with NO_2 and O_3, while its correlation with CO, PM_{10}, and SO_2 was insignificant. This was due to the fact that NO_2 and O_3 were identified as oxidation factors stimulating the respiratory system.

- According to the regression model and after adjusting the age as a confounding factor, O_3 was the most effective pollutant on daily admission of patients to hospital due to pulmonary disease.

- The variation trend of air pollution and daily admission of patient to hospital due to pulmonary disease were determined using time series analyses. According to this model, ARMA (1,1) was the best model showing better results in lag = 48 hours since the air pollutants, especially PMs delayed the effects on human health. Moreover, they are able to weaken the immunity system and develop other diseases.

Conflict of interest

The authors declare no conflict of interest regarding the publication of this research.

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