The effects of air pollutants on the mortality rate of lung cancer and leukemia

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Abstract. World Health Organization classifies air pollution as the first cause of human cancer. The present study investigated impact of air pollutants on the mortality rates of lung cancer and leukemia in Shiraz, one of the largests cities of Iran. This cross-sectional (longitudinal) study was carried out in Shiraz. Data on six main pollutants, CO, SO_2, O_3, NO_2, PM_{10} and $PM_{2.5}$, were collected from Fars Environmental Protection Agency for 3,001 days starting from 1 January, 2005. Also, measures of climatic factors (temperature, humidity, and air pressure) were obtained from Shiraz Meteorological Organization. Finally, data related to number of deaths due to lung and blood cancers (leukemia) were gathered from Shiraz University Hospital. Relationship between variations of pollutant concentrations and cancers in lung and blood was investigated using statistical software R and MiniTab to perform time series analysis. Results of the present study revealed that the mortality rate of leukemia had a direct significant correlation with concentrations of nitrogen dioxide and carbon monoxide in the air ($P<0.05$). Therefore, special attention should be paid to sources of these pollutants and we need better management to decrease air pollutant concentrations through, e.g., using clean energy respect to fossil fuels, better management of urban traffic planning, and the improvement of public transport service and car sharing.

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Introduction

Unplanned expansions of cities, along with economic development and to rising energy demand, have caused numerous environmental problems and serious risks for human health. Indeed, air pollution has always been a serious threat for society health and for environment on the global scale (1-3).

Industries, urban traffic and combustion of fossil fuels for energy production are main sources of most of the organic and mineral compounds, oxidants and acids, and fine particles. They play a significant role in air pollution of most of the urban areas (4).

Impact of air pollution on human health has been investigated for many years. Mechanisms through which air pollution affects human health are very complex and not yet fully understood (5).

Since nasal cavity is the most common route of entrance of pollutants into the body, the combinations of gases, fine particles and chemical compounds in the indoor and outside environments can have adverse effects on health. Moreover, respiratory mucosa is very vulnerable to degeneration. It is the first organ damaged in its functionality due to air pollution (6-10). However, the consequences of long-term exposure to air pollution have not been clarified.

Epidemiological researches confirmed there is a direct relationship among air pollution and respiratory disease symptoms, lung failure, chronic bronchitis and number of deaths due to respiratory problems (11).

Various epidemiological studies, carried out in the USA and Europe, showed that air pollution might increase risk of lung cancer (12) and the mortality rate due to cardiovascular strokes (13). Other studies, also conducted in USA, showed there is a direct relationship between rate of mortality and the amount of sulphate and other pollutants in the air (14).

Thus, air pollution has been declared by the World Health Organization (WHO) as one of main causes of human cancer (5).

PM_{10} plays a leading role in different respiratory symptoms. Indeed, they cause temporal alteration of lung function and, so, they cause increase of respiratory disease rate and hospital admissions and the morbidity rate of cardiovascular diseases (15-19).

In 2005 edition of Air Quality Guideline, WHO established that nitrogen dioxide (NO_2), ozone (O_3), sulfur trioxide (SO_3), and particulate matter (PM) are air pollutants that affect human health significantly (1). The Environmental Protection Agency (EPA) fixed National Ambient Air Quality Standards for six principal pollutants, which are called 'criteria' air pollutants (2).

Although, since the first decade of the 20th century, some air pollution control programs have been conducted in many industrially developed countries to preserve human health and prevent environmental pollution, actually air quality is daily getting worse in most developing countries (1). Due to growth of air pollution, the residents have an increased risk perception of respiratory diseases (20).

Shiraz is the third largest city of Iran in terms of extension also it is in a special geographical location (being enclosed by mountains). Shiraz has both a high density of industries near urban area and a major urban traffic. All these factors lead to air pollution increase in the city.

Therefore, the main aim of the present study was to investigate the relationship between air pollutants and mortality rate related to leukemia and lung cancer.

Materials and methods

Pollutant data. This longitudinal study was carried out in Shiraz. Data on six main air pollutants, CO, SO_2, O_3, NO_2, PM_{10} and $PM_{2.5}$ were obtained from Fars Environmental Protection Agency and these data are related to 3,001 measurement days starting from, 1 January, 2005. These data were collected from two fixed monitoring stations located at opposite points of the city (Kazeroon gate and Imam Hussein square). Moreover, the daily minimum, maximum and average measurements of climatic factors such as temperature, humidity, wind speed and air pressure were obtained from Shiraz Meteorological Organization. Additionally, we considered rainfall, sunshine hours and daily evaporation rate.

Although meteorological data were complete, data related to air pollutants had some missing days. Lack of measurements of some pollutants in different times may have different reasons including obstruction of the filter that measure specific pollutants, blackout of electricity due to technical reasons. Thus, when data were accessible from both stations, we used mean concentration of pollutants to be more accurate.

However, some days, no information was available from any station. We used statistical methods to forecast pollutant concentrations in these cases: i) time series method was used for prediction in case that missing data were <5% of the earlier period, e.g., data related to CO concentration were completed using this method. ii) Missing items, which were >5% of the earlier period, were predicted by these data and by nonlinear regression method.

In total, more than 2,000 different models were used for all variables in this study to complete data properly.

Finally, data related to number of deaths due to both lung cancer and leukemia, in the investigated period, were obtained from Shiraz University Hospital.

Table I. Fitting models for cancer data.

Sites of cancer	Models (p, d, q)
Lung cancer in male	NA[a]
Lung cancer in female	NA[a]
Lymphoid cancer in male	ARIMA (0,0,0)
Lymphoid cancer in female	ARIMA (0,0,0)
Myeloid cancer in male	NA[a]
Myeloid cancer in female	ARIMA (0,0,0)

[a]Not assigned. ARIMA, Auto Regression Integrated Moving Average.

Table II. Fitting models for air pollution data.

Air pollutant parameters	Models (p, d, q)
CO	IMA (0,1,8)
PM	ARMA (2,0,2)
NO	IMA (0,1,15)
NO_2	ARIMA (1,1,14)
NO_X	IMA (0,1,14)
O_3	IMA (0,1,11)

PM, particulate matter; NO_2, nitrogen dioxide; O_3, ozone; IMA, Integrated Moving Average; ARMA, Autoregressive Moving Average; ARIMA, Auto Regression Integrated Moving Average.

Table III. Fitting models for meteorological data.

Meteorological parameters	Models (p, d, q)
Minimum temperature	IMA (0,1,16)
Maximum temperature	ARIMA (2,1,14)
Mean temperature	ARIMA (1,1,12)
Minimum humidity	IMA (0,1,7)
Maximum humidity	ARIMA (1,1,2)
Precipitation	ARMA (1,0,7)
Sunshine	ARMA (1,0,3)
Evaporation	ARIMA (2,1,2)
Maximum wind velocity	IMA (0,1,2)

IMA, Integrated Moving Average; ARIMA, Auto Regression Integrated Moving Average; ARMA, Autoregressive Moving Average.

Statistical analysis. Principal component analysis was performed on the meteorological variables and three major factors, were selected. Based on this statistical model, maximum and minimum temperature, maximum humidity and evaporation were replaced only by mean temperature variable. The variables known as sunshine magnitude and rainfall level were replaced only by rainfall level. Additionally, the maximum wind speed was considered as a separate factor. Then, correlation of the above factors with pollutants and cancers was analyzed and the correlation coefficient was determined.

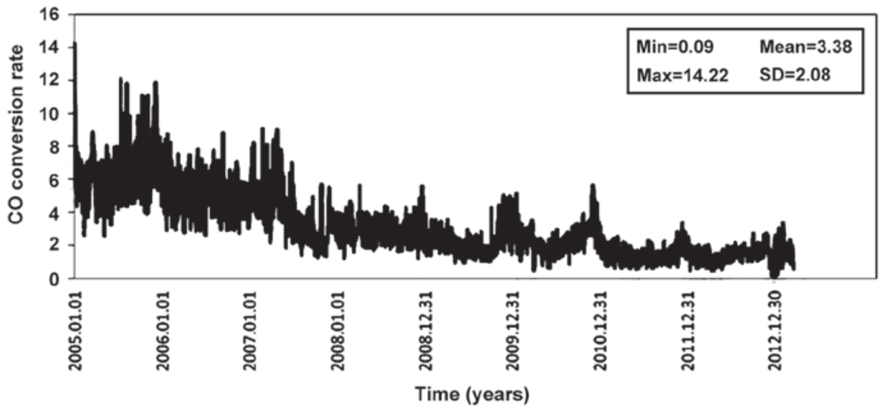

Figure 1. The variation of CO conversion rate during 2004-2012.

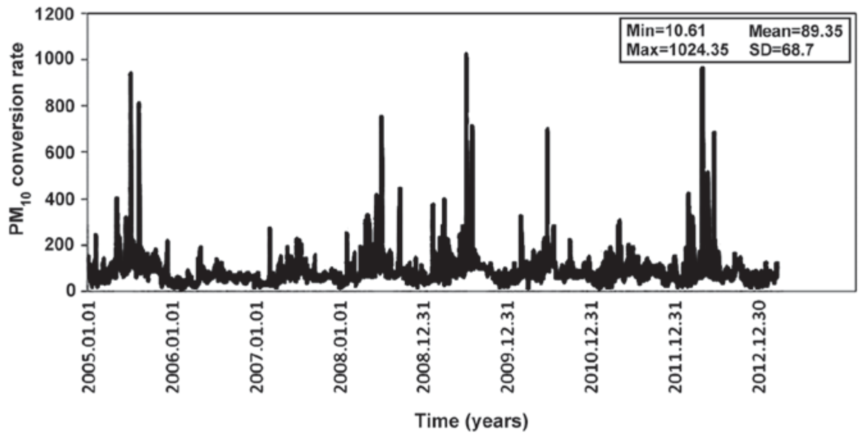

Figure 2. The variation of PM_{10} conversion rate during 2004-2012.

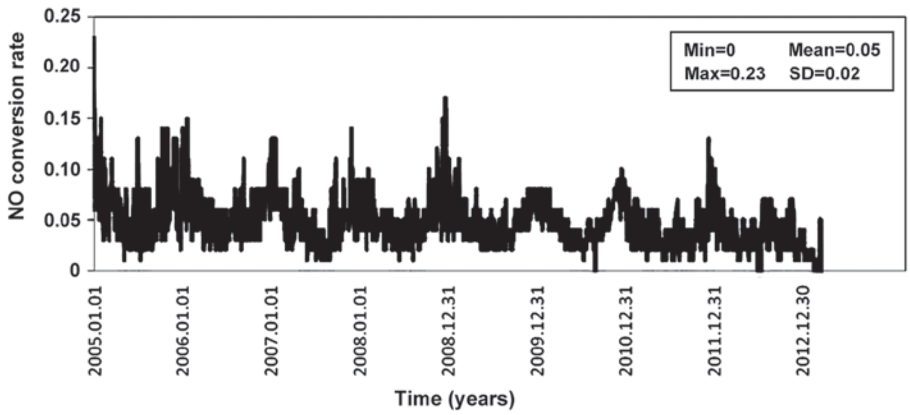

Figure 3. The variation of NO conversion rate during 2004-2012.

Autoregressive Moving Average (ARMA), Auto Regression Integrated Moving Average (ARIMA) and Moving Average, statistical models were used for the factor fluctuation modeling over time. $P<0.05$ indicates a statistically significant difference.

Results

Tables I-III show statistical analyses for cancer, air pollution, and meteorological parameters. As shown in Table I, the cancers studied in this survey did not match with any models. However, consistencies of air pollution and meteorological parameters are reported in Tables II and III.

Figs. 1-6 show variations in time of air pollutants more significantly for some studied substancies. As shown in figures, concentrations of CO, NO, NO_2 and NO_X decreased during the present study, while O_3 concentration increased. There was a periodic alteration of the CO, NO and NO_X concentrations. Peak of pollutant concentrations was in the tenth month

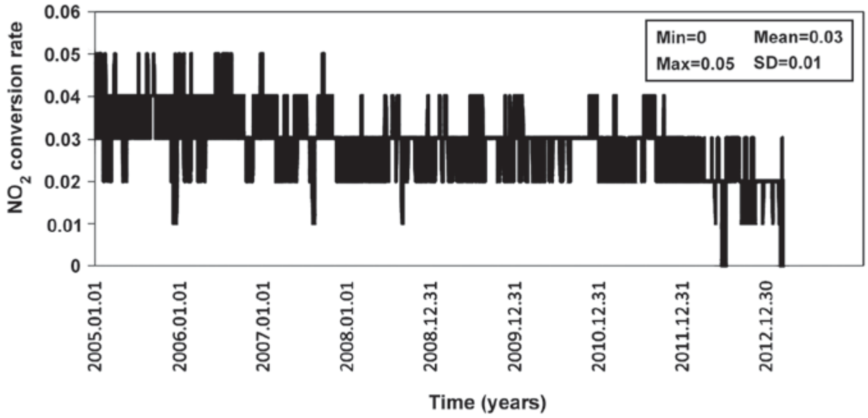

Figure 4. The variation of NO_2 conversion rate during 2004-2012. NO_2, nitrogen dioxide.

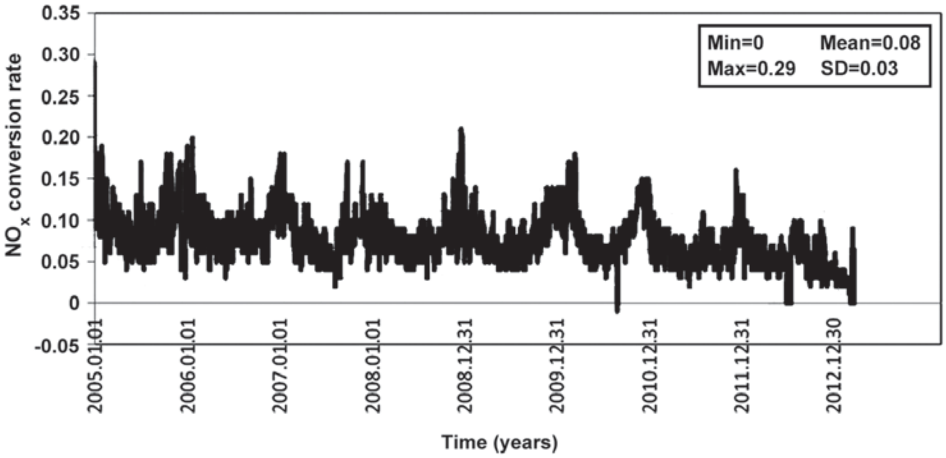

Figure 5. The variation of NO_X conversion rate during 2004-2012.

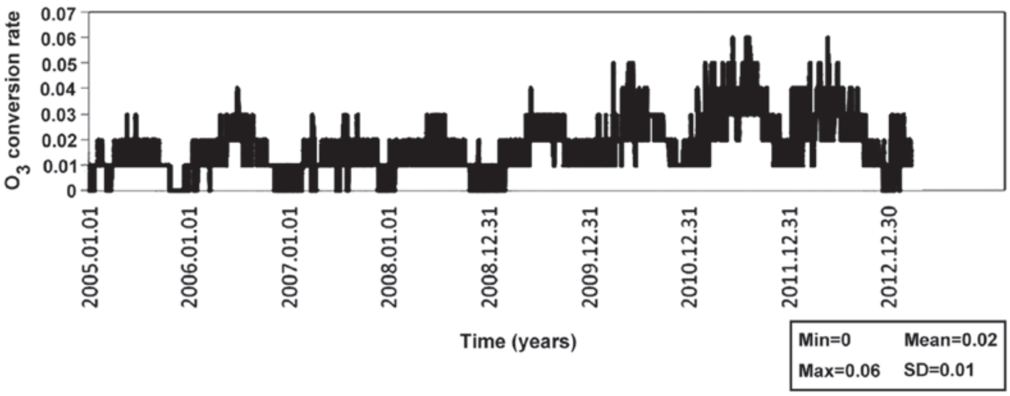

Figure 6. The variation of O_3 conversion rate during 2004-2012. O_3, ozone.

of each year. An extreme reduction occurred in subsequent six months. The trend of O_3 concentration was quite reverse compared to the other pollutants, with peak of concentrations in the warmer months. Indeed, no specific pattern was observed for NO_2 concentrations.

Figs. 7-9 show variation in time of weather conditions. Annually, highest rainfall level, the lowest temperature and the lowest wind speed occurred in the tenth month of each year. The lowest rainfall and the maximum temperature were observed approximately six months later.

Figs. 10-15 show the number of different cancer cases in the studied period. The above figures indicate that none of diseases follows a specific pattern. Also, average temperatures and precipitations level have no relationship with concentrations of CO. Instead, we observed the following relationships: i) both maximum wind speed and

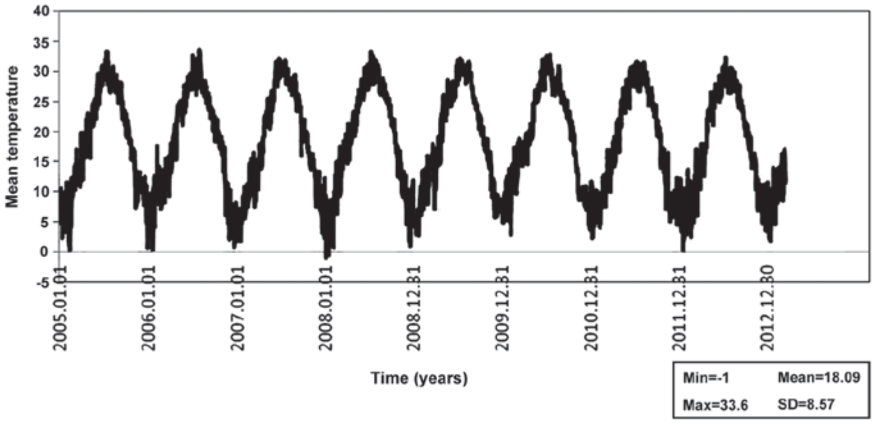

Figure 7. The variation of mean temperature during 2004-2012.

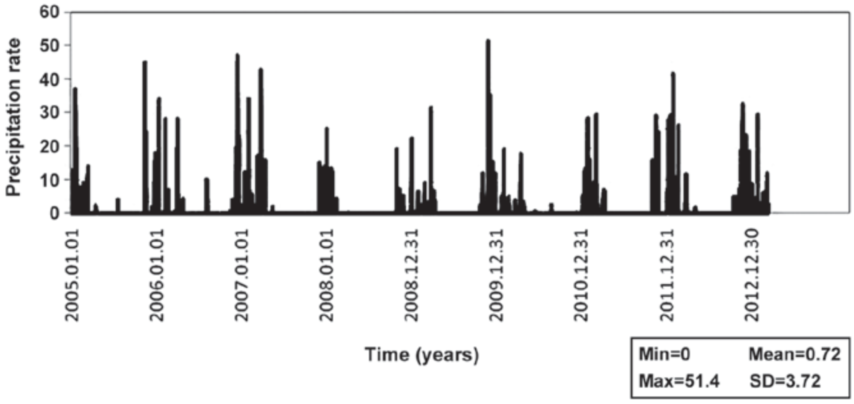

Figure 8. The variation of precipitation rate during 2004-2012.

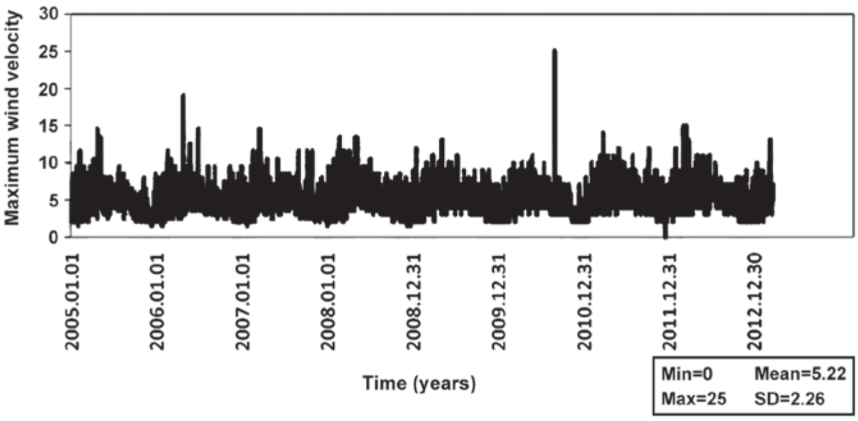

Figure 9. The variation of maximum wind velocity during 2004-2012.

NO_2 concentration have a weak but significant inverse linear relationship with lung cancer in men (P<0.001 and r<-0.079); ii) in the total population, lung cancer has a weak but significant inverse linear relationship with the maximum wind speed and NO_2 concentration (P<0.001 and r<-0.085); iii) lymphatic cancer in women has a weak but significant inverse linear relationship with concentration of NO_2 (P<0.001 and r<-0.052); iv) myeloid cancer in men has a weak but significant inverse linear relationship with NO_2 concentration (P<0.001 and r<-0.043); v) lymphoid cancer in men and women has a weak but significant inverse linear relationship with concentration of NO_2 (P<0.001 and r<-0.042); and vi) total cancers have a weak but significant inverse linear relationship with the maximum wind speed and NO_2 concentration (P<0.001 and r<-0.092).

Generally, it seems that concentration of NO_2 in Shiraz has a weak and inverse relationship with the mortality rate of lung and lymph node cancers. Furthermore, in some cases the

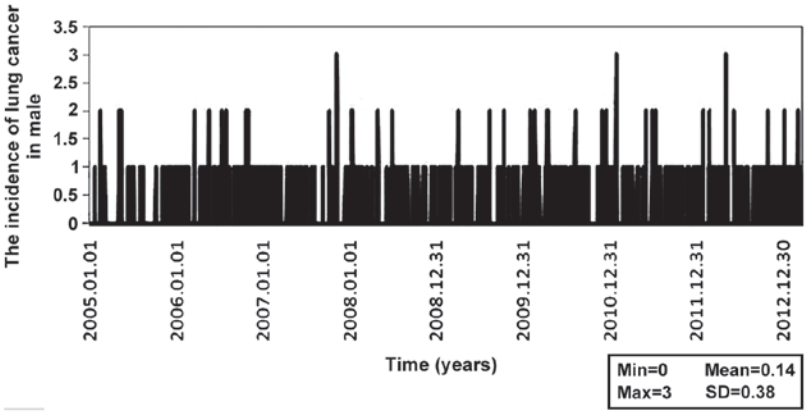

Figure 10. The incidence of lung cancer in men in 2004-2012.

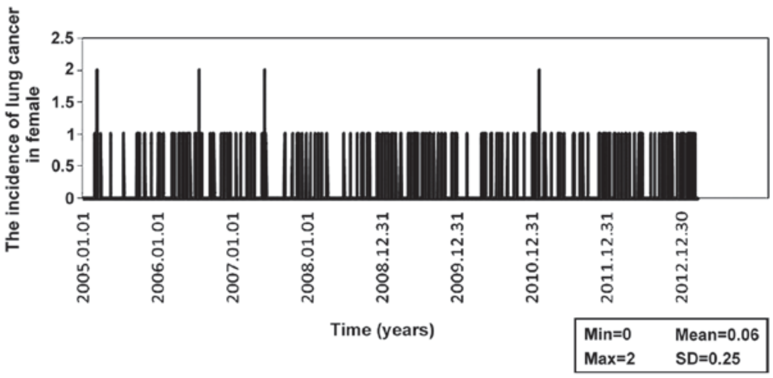

Figure 11. The incidence of lung cancer in women in 2004-2012.

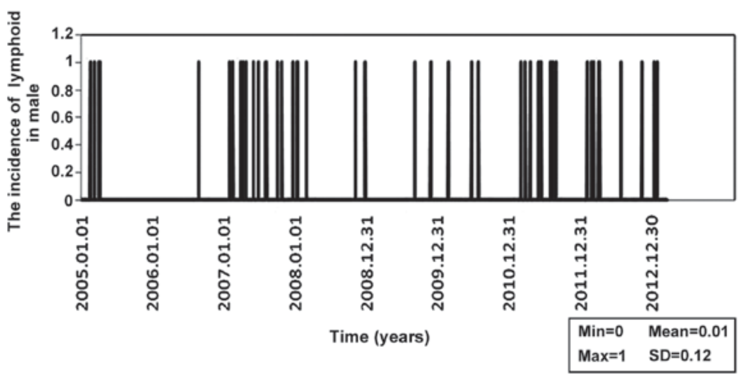

Figure 12. The incidence of lymphoid in men in 2004-2012.

maximum wind speed has the same relationship with mortality of lung and lymph node cancers.

According to our statistical analysis, it seems there is a weak relationship between the pollutant levels and the above mortality.

Discussion

The results of the present study indicated that the number of deaths due to lung cancer and leukemia had a weak but significant relationship ($P<0.05$) with the concentration of NO_2 and CO in the air.

Wong *et al* studied (5) epidemiological and experimental issues relating to genotoxic effects of air pollution and DNA reporting that due to the increasing number cases of lung cancer, it would be essential that governments pay special attention to all preventive measures to reduce air pollution, to develop clean energy programs, and to improve research on investigation of carcinogenesis effects of air pollution.

Study of Chalbot *et al* on $PM_{2.5}$ in USA in 2014 showed that implementation of law and air pollution regulations had major effects even in areas with high main risk factors of mortality as obesity and smoking (21).

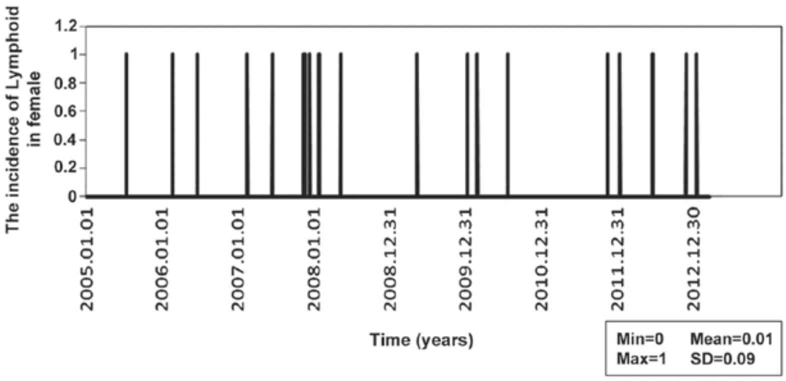

Figure 13. The incidence of lymphoid in women in 2004-2012.

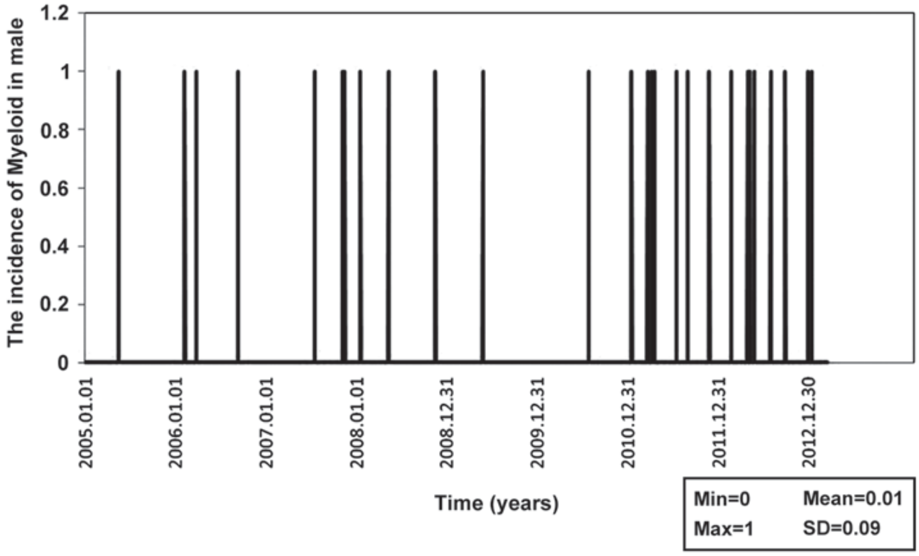

Figure 14. The incidence of myeloid in men in 2004-2012.

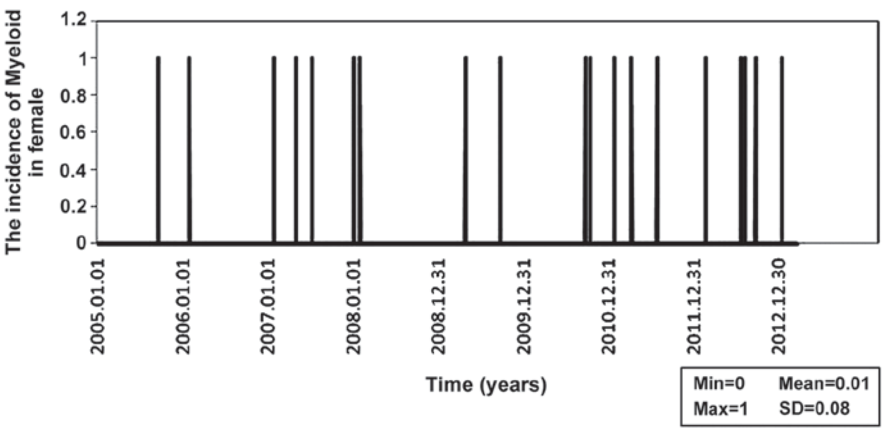

Figure 15. The incidence of myeloid in women in 2004-2012.

Pope *et al* revealed prolonged contact with fine particles by combustion was related to lung cancer and cardiovascular disease (13). Vineis and Husgafvel-Pursiainen demonstrated that air pollution increased lung cancer, especially in combination with some other known risk factors such as smoking, passive cigarette smoke, and occupational exposures. The present study also showed that organic air pollutants, especially PAH compounds, had genotoxic and oxidative effects on DNA (12).

Gilliland *et al* proclaimed that short-term changes in the amount of O_3 caused respiratory diseases that led to absence of 10-12-year-old children from school. Therefore, adverse effect of O_3 on children's health has been established (11). Previous studies carried out in Tehran city also showed that CO, SO_2 and NO_2 were the most important causes of deaths due to heart disease (7). Masjedi *et al* showed the concentrations of SO_2 and NO_2 had a significant correlation with asthma attacks in Tehran (22).

Previous studies in Ahwaz city carried out by Zolghi *et al*, using appropriate models, indicated that the percentage of deaths due to air suspending PM_{10} measured in 2010 was 17.5% which was 5.5% higher than the preceding year (23). Research in Australia, revealed that the most important reasons for hospital emergency admissions for respiratory disease were PM_{10} such as ozone concentrations (24).

The study of Lewis *et al* also showed the major reasons of hospital admission of children were asthma attacks due to high concentrations of $PM_{2.5}$ and ozone (25).

Moreover, Italian studies reported significant correlation between air pollution in urban area and risk of childhood leukemia (26,27).

However, the present study is unique as it shows the correlation among factors such as air pollutants, local meteorological conditions, and mortality rate due to cancer in Shiraz and help local authorities, politicians and all those involved in this topic to pay special attention to these issues and to control sources of air pollution such as industries and transport systems and to standardize use of fuels. Therefore, special attention should be paid to sources of these pollutants and we need better management to decrease air pollutant concentrations through, e.g., using clean energy in respect to fossil fuels, better managing of urban traffic planning, improved public transport service and car sharing.

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