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Title Page

Title of the article:

Short-term effects of air pollution on daily asthma-related emergency department visits in an Industrial City

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Abstract:

Background: Epidemiological studies from Europe and North America have provided evidence that exposure to air pollution can aggravate symptoms in asthmatic patients.

Objective: This study was designed to investigate the statistical association between exposure to air pollution and Asthma-related Emergency Department visits (AEDv) in a city in the Middle East.

Methods: Daily number of AEDv, air pollution levels (PM₁₀, PM_{2.5}, SO₂, NO₂ and CO) and meteorological variables were obtained from Jubail Industrial City, Saudi Arabia, for the period (2007-2011). Data were analyzed using a time-series approach. Relative risks (RRs) were estimated using Poisson regression.

Results: The associations between AEDv and PM₁₀, PM_{2.5}, SO₂ and NO₂ remained positive and statistically significant after mutual adjustment in the multi-pollutants model. The RR of AEDv increased by 5.4%, 4.4%, 3.4% and 2.2% per an inter-quartile range increase in SO₂ (2.0ppb), PM_{2.5} (36µg/m³), NO₂ (7.6ppb) and PM₁₀ (140µg/m³) respectively. No significant associations between AEDv and CO were found.

Conclusions: Current levels of ambient air pollution are associated with AEDv in this industrial setting in the Middle East. Greater awareness of environmental health protection and the implementation of effective measures to improve the quality of air in such settings would be beneficial to public health.

Main Text

BACKGROUND

Air pollution is a known risk factor for adverse cardio-respiratory health effects ¹. Time-series analyses have been used to estimate the influence of daily variations in air pollutant levels on daily counts of asthma-related admissions within a geographically defined population ^{2,3}. Several studies have identified an increase in asthma-related admissions associated with increases in Particulate Matter with diameter of 10 micrometers or less (PM₁₀) ⁴⁻¹⁶. These studies have reported a significant positive association between PM₁₀ levels and asthma-related hospital visits, with an increase of 10-90 $\mu\text{g}/\text{m}^3$ of PM₁₀ associated with an estimated increase of 0.1%-14% of asthma-related admissions.

Some studies reported on the relationship between exposure to Particulate Matter with diameter of 2.5 micrometers or less (PM_{2.5}) and hospital visits for asthma patients ^{4,10,11,17-22}. These studies indicate that an increase in PM_{2.5} level by 7-20 $\mu\text{g}/\text{m}^3$ was associated with increased asthma-related admissions of 3%-9%.

Other studies have considered the relationship between Nitrogen Dioxide (NO₂) levels and asthma-related admissions ^{4,6,8-11,13,16,17,20,23-26}. Most of these studies have reported a significant positive association between NO₂ levels and asthma-related hospital visits, with an increase in NO₂ levels by 9-27 $\mu\text{g}/\text{m}^3$ associated with an estimated 0.2%-9.0% increase in asthma-related admissions. In contrast, some studies found limited evidence for an association between the level of NO₂ and hospital admissions in single and multi-pollutants model ^{6,8,9,16}. These inconsistent results may be due to a high correlation

between NO₂ and other pollutants, such as Particulate Matter (PM), Carbon Monoxide (CO) and Sulphur Dioxide (SO₂) reported in previous studies ^{6,8,9,16}.

Several studies have reported on the association between exposure to SO₂ and hospital visits for asthma patients ^{4,6,9-11,13,16,20,23-27}. Most of these studies have reported a positive association with an increase in SO₂ levels by 10-50µg/m³ associated with an estimated increase of 1.1%-7.8% in asthma-related hospital admissions ^{4,6,11,20,23-25,27}. However, some studies found limited evidence for an association between the level of SO₂ and hospital admissions in single and multi-pollutants model ^{9,10,13,16,26}.

Little research on this topic has been carried out in the Middle East. Studies in Asian ²⁸ and Latin American countries ²⁹ with rapid urbanization and industrialization, where levels of air pollution and meteorological conditions are different from North America and Western Europe have also been carried out ³⁰. This study fills important gaps in our understanding of the influence of air pollutants levels on Asthma-related Emergency Department visits (AEDv) in an industrial city in Saudi Arabia.

METHODS

Study Location

This study was set in Al Jubail Industrial City, which is located in the Eastern Province. The Eastern province is the largest province in Saudi Arabia. The Kingdom's main oil and gas fields, onshore and offshore, are mostly located in the Eastern Province. In 1975, Jubail Industrial City was designated as a site for a new industrial city by the Saudi government, and has seen a rapid expansion and industrialization since. The industrial city hosts a global hub for chemical industries and the largest industrial city in the Middle East. It also holds the Middle East's largest and the world's fourth largest petrochemical company.

(<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3863874/>)

(<https://www.rcjy.gov.sa/en-US/Jubail/AboutCity/Pages/default.aspx>)

Air pollution and meteorological data

Hourly fixed-site air quality monitoring data for the period 1st January 2007 to 31st December 2011 were collected from the residential fixed-site monitoring station (site 8, coordinates of 27° 7'54.03"N 49°31'57.02"E) located within the community area in Jubail Industrial City, Saudi Arabia (See Supplemental Material; selection of fixed-site monitoring station, Table S1, Table S2 and Figure S1). The monitored pollutants include: PM₁₀, PM_{2.5}, SO₂, NO₂ and carbon monoxide (CO). The fixed-site monitoring station also measured hourly meteorological conditions including temperature (T), relative humidity (RH), wind speed (WS) and wind direction (WD). The daily missing value from the

residential fixed-site station (number 8) was replaced with the mean level of the remaining stations multiplied by a correction factor, which was the ratio of the seasonal mean (three months) for the missing station to the corresponding seasonal mean for the remaining stations on that particular day ³².

Data on asthma-related emergency department visits

The health data were obtained from the Royal Commission Health Service Program in Jubail Industrial City, which is responsible for the Royal Commission Hospital. Relevant records were identified based on a discharge diagnosis of asthma using the International Classification for Diseases, 9th revision (ICD-9 code 493). The data on AEDv were obtained for the period 1st January 2007 to 31st December 2011, for all ages.

Statistical analysis

The time-series analysis was conducted using Generalized Linear Models (GLM) with Poisson regression. The steps used to apply the GLM with Poisson regression were adopted from the method described by Tadano, et al. ⁵. Relative risks (RRs) were estimated using Poisson regression, while controlling for meteorological variables, day of the week and public holidays, for lag times of 0 - 7 days. The results were expressed as percent increase in AEDv (with 95% confidence intervals (95% CI)) per interquartile range (IQR; 75-25th percentile) increase of each pollutant. The original results used 7 degrees of freedom (*df*) per year for the natural cubic spline of temporal trend (See Supplemental Material; Time-series analysis: Akaike Information Criterion, Table S4).

Single and multiple pollutant models

After adjusting the GLM with Poisson regression, including all the time trends and explanatory variables, and choosing *df* that best fits the data, the fitted model was tested using the pseudo (R^2) and the chi-squared (X^2) statistic to ensure the best fit model was applied to create the single-pollutant model ^{5,31} (See Supplemental Material; Time-series analysis: Partial autocorrelation functions, Figures S2-S6 and Single-pollutant model, Tables S5-S6).

Multi-pollutant models were used to study the impact on AEDv of PM₁₀, PM_{2.5}, SO₂ and NO₂, adjusting for the other pollutants, as well as relative humidity, temperature and indicator variables for day of the week and holidays. Multi-pollutant models used the same basic steps as the single-pollutant model, with the inclusion of two or more pollutant variable terms ³². Pollutants that were significant in the single-pollutant analysis and the lag that had the strongest univariate effect were tested, using GLM with Poisson regression applied in R software.

RESULTS

Descriptive analysis

A total of 8434 AEDv occurred during the study period (Table 1). The time-series plots of daily AEDv revealed a prominent seasonal cycle as shown in Figure 1. The day-to-day variations in air pollutants levels of PM₁₀, PM_{2.5} and NO₂ also showed clear seasonal patterns. SO₂ levels increased steadily over years 2-4, but decreased over the last year

of the study period. CO did not show any seasonally or yearly trend, but variability in CO appears to decrease over the study period.

Comparisons of recorded air quality with Jubail Air Quality Standard (AQS) and WHO Air Quality Guidelines (AQG) are shown in Table 1. SO₂, PM_{2.5} and PM₁₀ exceeded the daily Jubail AQS and WHO AQG limits, while PM_{2.5} and PM₁₀ also exceeded annual Jubail AQS and WHO AQG limits for each of the five years.

AEDv were negatively correlated with PM₁₀ and PM_{2.5}, and positively correlated with NO₂ (See Supplemental Material; selection of fixed-site monitoring station, Table S3). A strong positive correlation was observed between PM₁₀ and PM_{2.5} ($r=0.816$, $p<0.01$). While, a weak but significant positive correlation was observed for NO₂ with CO and SO₂ ($r=0.258$ and $r=0.217$ respectively).

Comparisons of recorded air quality with and WHO Air Quality Guidelines (AQG) are shown in (Table 1). PM_{2.5} and PM₁₀ exceeded the daily and annual WHO AQG limits, and SO₂, exceeded only daily WHO AQG limits. However, NO₂, and CO did not exceeded the limit values.

Single and multi-pollutant models

All pollutants studied in the single and multi-pollutant model, except CO, were associated with an increase in daily AEDv as shown in Table 2. The lags associated with the most statistically significant increase in AEDv for PM₁₀, PM_{2.5} on the same day (lag 0), SO₂ after two days (lag 2) and NO₂ after three days (lag 3) from the single-pollutant model were subsequently considered in a multi-pollutant model. The relative risks

(together with 95% confidence intervals) for AEDv per IQR increase in pollutant concentration, after mutual adjustment for the remaining pollutants, are shown in Table 3. Owing to the multi-collinearity of PM₁₀ and PM_{2.5} (See Supplemental Material; selection of fixed-site monitoring station, Table S3), these pollutants were separately included in the multi-pollutant model. For SO₂ and NO₂, the result similar with either PM₁₀ or PM_{2.5}, and only the set of results with PM_{2.5} included in the multi-pollutant model is presented in Table 3 (it gave the highest RR for AEDv when compared with PM₁₀). The effects of these four pollutants appeared to be independent, as the associations remained significant after adjustment for the remaining pollutants which were simultaneously introduced (See Supplemental Material; the exposure-response association Figures S7).

DISCUSSION

Main finding of this study

The main results yielded by this study suggest that the risk of AEDv increased positively and with statistical significance with increasing ambient levels of PM_{2.5}, PM₁₀, SO₂ and NO₂ in the setting of the industrial city of Jubail, Saudi Arabia. The effects of these four pollutants were independent, as the associations remained significant after mutual adjustment.

PM₁₀

The most statistically significant increase in AEDv was a 2.2% increase (95% CI: 1.3, 3.2) associated with an IQR change in PM₁₀ levels ($140\mu\text{g}/\text{m}^3$) on the same day in the multi-pollutant model in the present study. This positive association is in line with findings of many of the previous studies of PM₁₀ and AEDv or asthma hospitalization for all ages at different lags from other areas of the world^{4,5,9,10,12,13}. The systematic review and meta-analysis by Zheng et al. published in 2015 reported a significant positive association between PM₁₀ and asthma-related emergency visits/hospitalization for all ages. This review, which included 51 studies for PM₁₀ in their meta-analysis, suggested that the RR increased 1.0% with a $10\mu\text{g}/\text{m}^3$ increase in PM₁₀ levels on lag day 1 in the single-pollutant model⁴. Similarly, a statistically significant relationship was detected in single-pollutant model for asthma-related emergency visits/hospitalization for all ages in Sao Paulo, Brazil (a 5.0% increase in hospital visits per $90\mu\text{g}/\text{m}^3$ increase in PM₁₀ levels on lag day 3⁵); in Taipei, Taiwan (a 4.5% increase in hospitalizations per $28\mu\text{g}/\text{m}^3$ increase in PM₁₀ levels on lag day 3⁹); in Madrid, Spain (a 3.9% increase in hospitalizations per $10\mu\text{g}/\text{m}^3$ increase

in PM₁₀ levels on lag day 3¹³); in Atlanta, USA (a 3.9% increase in hospitalizations per 10 μ g/m³ increase in PM₁₀ levels on lag day 3¹²); in Hong Kong, China (a 1.9% increase in hospitalizations per 10 μ g/m³ increase in PM₁₀ levels on lag day 0-5¹⁰). These previous studies have only generated the results from the single-pollutant model which are likely confounded, at least in part, by correlated pollutants¹². Possible explanations for differences in the RR results in these previous studies are the study designs, timeframe and city, as different regions may have divergent pollutant mixtures^{9,33}.

However, the results presented in this study did not show a correlation between PM₁₀ and CO, SO₂ and NO₂, and the estimated effect remained significant after further adjustment for SO₂ and NO₂ in the multi-pollutant model. This indicates that PM₁₀ is not acting as a proxy for other pollutants, but rather points to an independent association.

PM_{2.5}

In the current study, the most significant increase in AEDv was 4.4% (95% CI: 2.4, 6.6) per IQR change of PM_{2.5} level (36 μ g/m³) on the current day. This finding is consistent with those of other studies, which reported a positive association between PM_{2.5} levels and asthma-related emergency visits/hospitalization for all ages at different lags^{4,9,10,17-19,22}. A statistically significant increase in AEDv (1.5% per 10 μ g/m³ increase in PM_{2.5} levels on lag day 1) was detected in a meta-analysis from 2016 which included 16 studies from developed countries, with 13 studies from the USA and the other three from Canada, Finland and Taiwan¹⁹. Similarly, a systematic review and meta-analysis conducted in 2015 observed a significant positive association between PM_{2.5} and asthma-related emergency visits/hospitalization for all ages, which included 37 studies for PM_{2.5} in their

meta-analysis, RR increased 2.3% with a $10\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ levels on lag day 1 in the single-pollutant model ⁴. Also, a statistically significant relationship was reported in single-pollutant model for asthma-related emergency visits/hospitalization for all ages in Beijing, China (0.51% per $10\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ levels on lag day 1 ¹⁸); in Erie County, NY/USA (6.8% per IQR change ($6.20\mu\text{g}/\text{m}^3$) on lag day 2 ¹⁷); in Tacoma, Washington/USA (4% per IQR change ($7\mu\text{g}/\text{m}^3$) on lag day 2 ²²); and in Hong Kong, China (2.1% per $10\mu\text{g}/\text{m}^3$ increase in PM_{10} levels on lag (0-5) days ¹⁰). In contrast, a study conducted in Taipei, Taiwan, did not observe an association between AEDv for asthma and $\text{PM}_{2.5}$ (IQR = $20.2\mu\text{g}/\text{m}^3$) in the single-pollutant model ⁹. However, these previous studies did not report results from multi-pollutant models which are necessary if we are to determine which pollutants contribute to the association ³⁴. The reported RR results of $\text{PM}_{2.5}$ and asthma-related emergency visits/hospitalization from the previous studies may be inconsistent due to differing exposure sources, climate factors, seasonal patterns and related pathways which affect emissions, composition and kinetics of pollutants ^{9,33-35}.

SO₂

The most significant increase in AEDv was 10.3% (95% CI: 4.6, 16.3) for all ages associated with a $10\mu\text{g}/\text{m}^3$ increase in SO_2 on lag day 2 in the multi-pollutant model in the present study. This positive association supports previous research, which reported a positive association between SO_2 levels and asthma-related emergency visits/hospitalization for all ages at different lags ^{4,24,4,10,13,24,25}. A systematic review and meta-analysis of 65 studies conducted in 2015 observed 1.1% increase in RR in asthma-related emergency visits/hospitalization for all ages per $10\mu\text{g}/\text{m}^3$ increase in SO_2 levels on lag day 0 in the single-pollutant model ⁴. Similarly, a statistically significant relationship

was detected in single and multi-pollutants model for asthma-related emergency visits/hospitalization for all ages in a study conducted in Cartagena, Spain, which found a 5.2% (95% CI: 1.4, 11.0) increase in asthma visits for all ages per $10\mu\text{g}/\text{m}^3$ increase in SO_2 levels at lag day 4 ²⁴.

Other studies have reported no significant effect of SO_2 on asthma visits ^{9,10,13,15,25-27}. Most of these studies have reported an interaction between SO_2 levels and other pollutants such as PM, CO and NO_2 due to collinearity among pollutants generated by the same sources ^{9,10,13,20,27}. This can result in removal of statistical significance of SO_2 in the multi-pollutant model. The estimated effect in the current study remained significant after adjustment for $\text{PM}_{2.5}$ and NO_2 in the multi-pollutant model, which suggests that SO_2 may not simply act as a proxy for other pollutants, but has an independent effect. In addition, the results of most controlled-chamber experiments with asthmatics have consistently shown that they are more sensitive to SO_2 than non-asthmatics ^{26,36}, lending plausibility to there being an independent effect of SO_2 on asthma/asthma exacerbation.

NO_2

The most significant increase in AEDv was at lag day 3 (2.4% (95% CI: 0.5, 4.2) per a $10\mu\text{g}/\text{m}^3$ increase in NO_2 levels in the current study. This positive association agrees with other studies that observed similar associations for all ages on different lag days ^{4,13,17,24}. A systematic review and meta-analysis of 66 studies conducted in 2015 observed a significant positive association between NO_2 and asthma-related emergency visits/hospitalization for all ages (RR increased 1.8% per $10\mu\text{g}/\text{m}^3$ increase in NO_2 levels on lag day 0 in the single-pollutant model ⁴). Another recent study conducted in Erie

County, NY/USA, also showed a similar positive effect (a 7.8% increase in asthma visits at lag day 1 per IQR change in NO₂ (17.7µg/m³)¹⁷). Furthermore, a study conducted in Cartagena, Spain, detected a positive association in single and multi-pollutants model (2.6% (95% CI: 1.4, 11.0) increase in asthma visits for all ages per 10µg/m³ increase in NO₂ levels at lag day 4²⁴). Similarly, another study conducted in Madrid, Spain, reported a 3.3% increase in asthma visits at lag day 3 for all ages per 10µg/m³ increase in NO₂ level in single-pollutant model¹³.

Conversely, a study in Taipei, Taiwan, found no statistically significant association for asthma visits for all ages with NO₂⁹. Likewise, studies of asthmatic children visits and NO₂ levels in Athens, Greece,⁶ Milan-Italy⁸ and Seattle, USA,¹⁶ found no significant associations. These inconsistent results may be due to a high correlation between NO₂ and other pollutants, such as PM, CO and SO₂ reported in previous studies^{6,8,9,16}. Hence, NO₂ could be a marker of other pollutants generated by traffic-related sources, such as PM^{14,25}. However, the estimated risk shown in this study in Jubail remained unaltered on inclusion of the other pollutants in the multi-pollutant model, suggesting that NO₂ may be independently associated with AEDv. Asthmatics are the most responsive group to nitrogen dioxide studied to date, although controlled studies on the effects of short-term exposure on the symptoms and severity of asthma have not led to clear-cut findings³⁶. Panel studies among asthmatic subjects show acute health effects when exposure to NO₂ at levels higher than 500µg/m³, and one meta-analysis has indicated effects at levels exceeding 200µg/m³³⁶. This suggests that the observed association with ambient NO₂ levels in the general population may be plausible^{25,36}.

CO

Our study did not find a statistically significant association between daily CO levels and AEDv. The lack of association observed in this study supports previous works conducted in Erie County, NY/USA ¹⁷, Taipei, Taiwan ⁹ and Milan, Italy ⁸. However, a significant positive effect of CO on asthma visits was found in two previous studies conducted in two cities within the USA; Tacoma ²² and Seattle ¹⁶. These studies reported that an IQR increase in CO levels of 0.6ppm in Tacoma and 0.7ppm in Seattle resulted in 10% (95% CI: 2.0, 19.0) and 3.0% increase (95% CI: 0.1, 6.0) in AEDv, respectively. These previous studies have only generated the results from the single-pollutant model which are likely confounded, at least in part, by high correlations between CO and particulates which range between 0.74 in Tacoma and 0.82 in Seattle. CO has no biological plausible mechanism for exacerbation of asthma, so this effect is interpreted as being related to traffic air pollution, and not to CO itself ^{16,22}.

Limitations of this study

Similar to other ecological time-series studies, this study was limited by the fact that precise individual level of exposure to a specific pollutant could not be assessed.

Although many important confounding variables have been controlled in the analysis, further adjustment of other confounders such as pollens and aeroallergens which may be alter the associations between AEDv and air pollution, would be desirable. Some studies have observed that pollen and aeroallergens could precipitate the exacerbation of asthma ^{24,37}, whereas other studies have not ^{13,38}. It was not possible to include pollen in the present study, but we would encourage this to be the focus of further works ²¹.

There is experience around the world, especially from developed countries, that can be drawn on regarding effective industrial, environmental and health policy. Until air quality issues are resolved, the levels of air pollutants should be incorporated into weather forecasts and alerts, as is practiced elsewhere ^{39,40}, so as to inform populations at risk, which may enable individuals to reduce their risks from outdoor air pollution.

What is already known on this topic?

There is a growing literature on time-series studies of air pollution and asthma-related admissions for populations in North America and Western Europe, little research on this topic has been carried out in the Middle East. Importance of this study is that to the best of our knowledge, this study is the first to investigate the association between air pollution and Asthma-related Emergency Department visits (AEDv) in an industrial city in Saudi Arabia.

What this study adds?

- Levels of PM_{2.5}, PM₁₀, SO₂ and NO₂, were associated with an increase in daily AEDv.
- No significant associations between AEDv and CO were found.
- PM_{2.5} and PM₁₀ exceeded daily and annual WHO air quality guidelines limits.

Conclusions

The present study in the setting of an industrial city in Saudi Arabia has revealed that risks of AEDv increased with increasing ambient levels of PM₁₀, PM_{2.5}, SO₂ and NO₂. The effects of these four pollutants appeared independent, effect sizes were in line with those

reported from other areas of the world. The current air quality standards in Jubail Industrial City might not be sufficient to protect public health in this setting. This calls for greater awareness of environmental protection and the implementation of effective measures to improve the quality of air.

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Table titles:

Table 1: Descriptive Statistics for Daily Asthma-related Emergency Department visits, Air Pollution and Meteorological Variables in Jubail Industrial City, Saudi Arabia, for the period 2007-2011

Table 2: Relative Risks (95% Confidence Interval for AEDv Per IQR Change in Pollutants Concentration for 0-7 Lag Days in The Single-Pollutant Model in Jubail Industrial City, Saudi Arabia, for the Period 2007-2011

Table 3: Relative Risks (95% Confidence Interval for AEDv Per Increase in Pollutants Concentration for 0-7 Lag Days in the Multi-Pollutant Model in Jubail Industrial City, Saudi Arabia, for the Period 2007-2011

Figure legends:

Figure 1: Time-series plots of daily AEDv and air pollutants for the period 2007-2011

Table 1: Descriptive Statistics for Daily Asthma-related Emergency Department visits, Air Pollution and Meteorological Variables in Jubail Industrial City, Saudi Arabia, for the period 2007-2011

	AEDv	PM ₁₀ ($\mu\text{g}/\text{m}^3$)	PM _{2.5} ($\mu\text{g}/\text{m}^3$)	SO ₂ (ppb)	NO ₂ (ppb)	CO (ppm)	Temp (°C)	RH (%)	
Total number of days	1826	1764	1786	1788	1793	1794	1793	1793	
Missing days*	0	62	40	38	33	32	33	33	
Mean	4.60	220.16	64.61	3.06	15.48	0.46	26.39	49.69	
Median	4	129.56	45.63	2.74	14.39	0.43	27.53	49.69	
Standard Deviation	3.30	308.49	64.52	1.80	6.37	0.19	8.02	15.18	
Minimum	0	2.00	9.96	0.01	0.07	0.02	6.33	12.94	
Maximum	28	3599.26	643.70	14.11	45.95	1.49	39.13	95.30	
Quartiles	25%	2	81.60	32.13	1.96	11.04	0.32	19.21	37.69
	50%	4	129.56	45.63	2.74	14.39	0.43	27.53	49.69
	75%	6	222.35	68.41	3.95	18.63	0.57	33.97	61.26
IQR	4	140.75	36.28	1.99	7.59	0.25	14.76	23.57	
Air Quality Exceedance (WHO, AQQ)	Daily	1618 (88.6%) days exceeded limit value (50 $\mu\text{g}/\text{m}^3$)	1623 (88.9%) days exceeded limit value (25 $\mu\text{g}/\text{m}^3$)	43 (2.3%) days exceeded limit value (7.7ppb)	Did not exceeded	Did not exceeded	Did not exceeded	Did not exceeded	
	Annual	All five years exceeded limit value (20 $\mu\text{g}/\text{m}^3$)	All five years exceeded limit value (10 $\mu\text{g}/\text{m}^3$)	Did not exceeded	Did not exceeded	Did not exceeded	Did not exceeded	Did not exceeded	

*Days excluded due to missing data ($\geq 75\%$ of the hourly values per day)

**N.A = Not applicable

List abbreviations: AEDv=Asthma-related Emergency Department visits, PM₁₀= Particulate Matter with diameter of 10 micrometers or less, PM_{2.5}= Particulate Matter with diameter of 2.5 micrometers or less, SO₂=Sulphur Dioxide, NO₂=Nitrogen Dioxide, Co=Carbon Monoxide, Temp=Temperature, RH=Relative Humidity, IQR=Inter-Quartiles Range, $\mu\text{g}/\text{m}^3$ =micrograms per cubic meter, ppb=parts per billion, ppm=parts per million, °C= degrees Celsius, %=percentage, WHO,AQQ= World Health Organization, Air Quality Guidelines

Table 2: Relative Risks (95% Confidence Interval for AEDv Per IQR Change in Pollutants Concentration for 0-7 Lag Days in The Single-Pollutant Model in Jubail Industrial City, Saudi Arabia, for the Period 2007-2011

Pollutant	Lag days	Relative Risk (95% CI)	T value
PM ₁₀ IQR (140µg/m ³)	0#	1.023 (1.014, 1.033)	4.71*
	1	1.011 (1.001, 1.022)	2.19*
	2	1.003 (0.992, 1.014)	0.51
	3	0.996 (0.985, 1.007)	-0.68
	4	0.997 (0.985, 1.008)	-0.60
	5	1.004 (0.993, 1.016)	0.73
	6	1.003 (0.992, 1.014)	0.54
	7	0.984 (0.973, 0.996)	-2.65
PM _{2.5} IQR (36µg/m ³)	0#	1.037 (1.026, 1.049)	6.31*
	1	1.019 (1.007, 1.031)	3.09*
	2	0.997 (0.985, 1.010)	-0.42
	3	0.989 (0.976, 1.002)	-1.62
	4	0.995 (0.982, 1.009)	-0.70
	5	1.006 (0.993, 1.020)	0.92
	6	0.995 (0.982, 1.009)	-0.70
	7	0.975 (0.962, 0.989)	-3.47
SO ₂ IQR (2.0ppb)	0	1.040 (1.010, 1.071)	2.61*
	1	1.052 (1.022, 1.083)	3.44*
	2#	1.058 (1.028, 1.089)	3.84*
	3	1.039 (1.009, 1.070)	2.54*
	4	1.004 (0.997, 1.011)	2.12
	5	1.003 (0.996, 1.010)	2.38
	6	1.002 (0.995, 1.009)	3.20
	7	1.003 (0.996, 1.010)	2.09
NO ₂ IQR (7.6ppb)	0	1.001 (0.975, 1.029)	0.10
	1	1.031 (1.005, 1.058)	2.38*
	2	1.015 (0.990, 1.042)	1.18
	3#	1.036 (1.010, 1.062)	2.71*
	4	1.002 (0.998, 1.005)	1.07
	5	1.012 (0.986, 1.038)	0.87
	6	1.008 (0.982, 1.034)	0.62
	7	1.010 (0.984, 1.037)	0.78
CO IQR (0.25ppm)	0	0.963 (0.933, 0.993)	-2.38
	1	0.962 (0.932, 0.993)	-2.42
	2	0.982 (0.952, 1.014)	-1.12
	3	1.007 (0.975, 1.039)	0.41
	4	0.983 (0.952, 1.014)	-1.09
	5	0.999 (0.968, 1.031)	-0.05
	6	0.990 (0.960, 1.022)	-0.62
	7	0.987 (0.960, 1.014)	-0.95

*Statistically Significant ($P < 0.001$).

#The better model after control for seasonality, temperature, humidity, day of the week and holidays.

List abbreviations: AEDv=Asthma-related Emergency Department visits, PM10= Particulate Matter with diameter of 10 micrometers or less, PM2.5= Particulate Matter with diameter of 2.5 micrometers or less, SO2=Sulphur Dioxide, NO2=Nitrogen Dioxide, Co=Carbon Monoxide, IQR=Inter-Quartiles Range, $\mu g/m^3$ =micrograms per cubic meter, ppb =parts per billion, ppm =parts per million, CI=Confidence Interval, %=percentage

Table 3: Relative Risks (95% Confidence Interval for AEDv Per Increase in Pollutants Concentration for 0-7 Lag Days in the Multi-Pollutant Model in Jubail Industrial City, Saudi Arabia, for the Period 2007-2011

Multi-pollutant model [#]	Lag days	Relative Risk (95% CI)		T value
		Per IQR	Per 10 $\mu\text{g}/\text{m}^3$	
PM ₁₀ Adjusted for SO ₂ and NO ₂	0	1.022 (1.013, 1.032)	1.002 (1.001, 1.003)	4.50*
PM _{2.5} Adjusted for SO ₂ and NO ₂	0	1.044 (1.024, 1.066)	1.012 (1.007, 1.018)	4.24*
SO ₂ Adjusted for PM _{2.5} and NO ₂	2	1.054 (1.024, 1.085)	1.103 (1.046, 1.163)	3.60*
NO ₂ Adjusted for PM _{2.5} and SO ₂	3	1.034 (1.008, 1.061)	1.024 (1.005, 1.042)	2.54*

*Statistically Significant ($P < 0.001$).

[#]Owing to the multi-collinearity of PM₁₀ and PM_{2.5}, they were separately put into the multi-pollutant model. For SO₂ and NO₂, the result is similar when putting either PM₁₀ or PM_{2.5}, and only the set of results when PM_{2.5} was included in the multi-pollutant model is presented.

List abbreviations: AEDv=Asthma-related Emergency Department visits, PM₁₀= Particulate Matter with diameter of 10 micrometers or less, PM_{2.5}= Particulate Matter with diameter of 2.5 micrometers or less, SO₂=Sulphur Dioxide, NO₂=Nitrogen Dioxide, Co=Carbon Monoxide, $\mu\text{g}/\text{m}^3$ =micrograms per cubic meter, *ppb*=parts per billion, *ppm*=parts per million, CI=Confidence Interval, %=percentage, IQR – Inter-Quartile Range; PM₁₀ IQR (140 $\mu\text{g}/\text{m}^3$), PM_{2.5} IQR (36 $\mu\text{g}/\text{m}^3$), SO₂ IQR (2.0*ppb*) and NO₂ IQR (7.6*ppb*).