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Air Pollution, Cardiovascular and Respiratory Admissions in Klang Valley, Malaysia - Finding the Effects

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ABSTRACT

This study aims to determine the association and risk of daily fluctuations of air pollution parameters in Klang Valley, Malaysia, with cardiovascular and respiratory admissions. The data on admissions and air pollution concentrations were obtained from various government agencies in Malaysia. The associations were estimated using a time series analysis of Poisson regression. The effects for every $10\mu/m^3$ increase in pollutants were reported as Relative Risk (RR). SO_2 showed the highest association with immediate effects at lag 0 for all cardiovascular admissions followed by NO_2. Gaseous pollutants of SO_2 and NO_2 showed a higher risk among elderly more than 60 years old. Immediate effects were found in both genders, with higher risks observed in males. NO_2 continues to be suggestively associated with all respiratory admissions. Children less than 9 years old presented a higher risk of NO_2 at various lag times with the highest value at lag0, followed by PM_{10}. Stratified analysis showed an incremental risk of respiratory admissions for males exposed to NO_2 compared to females. We found noteworthy associations for overall and age-specific admissions of cardiovascular and respiratory with the pollutants. Compared to particulates pollutant, gaseous pollutants showed a higher risk in both admissions.

INTRODUCTION

Air pollution has been identified as one of the world's major environmental adverse health effects concerns (Mahiyuddin et al. 2013, Tajudin et al. 2019). Common air pollutants included particulate matters (PM_{10} and $PM_{2.5}$), carbon monoxide (CO), ozone (O_3), sulfur and sulfur dioxide (SO_2), nitrogen oxides (NO_2), heavy metals, pesticides, volatile organic compounds, acid gases, solvents, radiation and bioaerosols (Sentian et al. 2019). These undesirable materials come from anthropogenic sources such as mobile, stationary, agricultural, and natural (Usmani et al. 2020, Amato et al. 2019). These harmful materials may harm human and ecosystem health, and the built environment, and lead to economic loss (Li et al. 2016, Rovella et al. 2021). Many epidemiological studies in all parts of the world have shown significant associations between air pollution and human morbidity, including in multi-cities studies, mainly affecting respiratory and circulatory systems (Phosri et al. 2019, Slama et al. 2019).

Different studies in various parts of the world revealed that cerebrovascular admissions were suggestively associated with short-term effects of NO_2 (Tajudin et al. 2019), particulate matter 10 micrometers or less in diameter (PM_{10}) (Moolgavkar 2000), O_3, CO and particulate matter 2.5 micrometers or less in diameter ($PM_{2.5}$) (Chan et al. 2006). In Malaysia, Mahiyuddin et al. (2013) conducted the first study on the health effects of air pollution using time series analysis to determine the association between air pollution and mortality in urban areas. Findings showed that O_3, CO, and PM_{10} were the pollutants that were found to be significantly associated with natural and respiratory mortality. This is also similar to what was reported by Tajudin et al. (2019).

Since the 1980's Malaysia faced frequent episodes of haze and most of them were the major episodes (Usmani et al. 2020). The sources could be either local or transboundary, such as forest fire from Indonesia (Sentian et al. 2019, Awang et al. 2000). Haze comprised high concentrations of PM_{10}, metal (Fe) ions, and zinc (Zn) together with gaseous (Usmani et al. 2020). The cost of medical care, especially inpatient hospital care in Malaysia increases tremendously. The results from Hassan et al. (2000), showed that limited activity days contributed to about 79.3% of the health damage costs, followed by an asthma attack, which contributed 10.7%. Other less significant health effects were respiratory, hospital admission, emergency room visits, and chronic bronchitis which contributed to total health damage cost estimated at Ringgit Malaysia (RM) 129 million (RM36-RM258 range).

This study aimed to obtain the risk estimates of pollutants towards cardiovascular and respiratory admissions in Malaysia's most urbanized area. This study differs from other time series studies on admissions and air pollution because it utilizes data from all main public hospitals in the Klang Valley area.

MATERIALS AND METHODS

Air Quality and Meteorological Data

The air quality data from 1st January 2008 to 31st December 2010 were obtained from the Department of Environment, Malaysia (DOE). The air pollutant parameters utilized in this study were PM_{10}, CO, SO_2, NO_2 and O_3. There were 52 continuous air quality monitoring stations (CAQMs) in Malaysia with six located in Klang Valley at Cheras, Kajang, Shah Alam, Klang, Gombak, and Petaling Jaya. The daily average for the pollutants was used to represent the daily concentration of pollutants concentrations for Klang Valley.

Data on meteorological parameters in Klang Valley were gained from two stations by Malaysia Meteorological Department. The data components were a daily 24 h average of temperature, relative humidity, and rainfall. Fig. 1 showed the locations of CAQMs and meteorological stations in Klang Valley.

Study Area

Klang Valley is one of the most industrialized areas following fast urbanization and is a densely populated region (Hassan et al. 2000). It is the most susceptible region exposed to air pollution compared to other regions of the country (Rahman et al. 2015, Juneng et al. 2011). Situated with mountains in the east and the Straits of Malacca in the west, this basin provides a conducive environment for pollutants to mount up, particularly when the meteorological condition is stable. Klang Valley has a 2832 km^2 area with

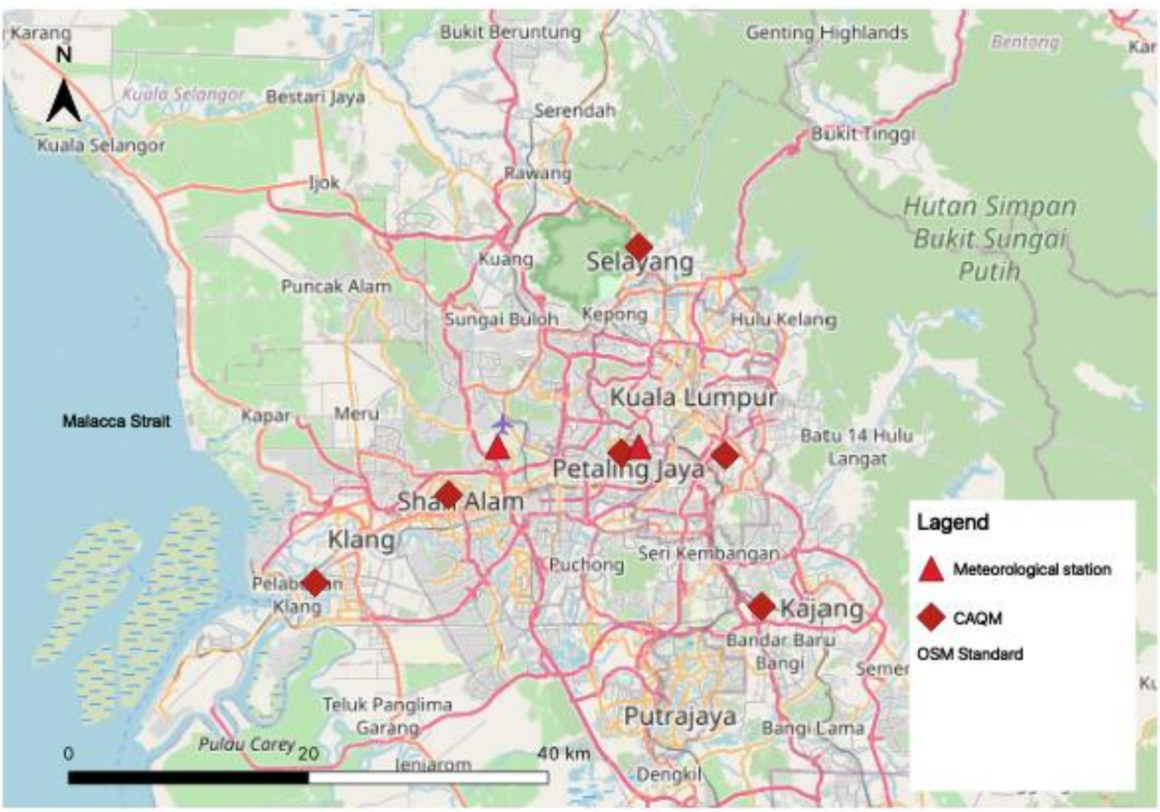

Fig. 1: Locations of continuous air quality monitoring stations (CAQMs) and meteorological stations in Klang Valley.

a total population of 7.9 million (UN World Urbanization Prospects 2021).

Hospital Admissions Data

Daily hospital admissions data between 1st January 2008 and 31st December 2010 was obtained from Health Informatics Centre, Ministry of Health's (MOH) database. Nine public hospitals in Klang Valley were selected for this study. The date of the patient's discharge from the hospital for which the diagnosis was classified according to the International Classification of Disease, Tenth Revision (ICD10) was assumed to be the date of disease diagnosis. The diseases selected for these studies were respiratory (J00-J99) and cardiovascular diseases (I00-I99). The data taken was anonymous.

Modeling and Statistical Analysis

Generalized Additive Model (GAM) with Poison time series regression was applied to examine the short-term effects of daily air pollutants on cardiovascular and respiratory admissions. The time variable representing the day, ambient temperature, relative humidity, total rainfall, day of the week, and holiday coding were the covariates used in the models. The time variable of the day was used to control for systematic variations by time in the data. Natural spline smoothing functions were used to control for long-term trends and seasonality from the admissions or other time-varying covariates that could confound the estimates of risk between admissions and pollutants. This study follows a similar methodology as what was done by Mahiyuddin et al. (2013) and Wong et al. (2008). A partial autocorrelation function (PACF) plot of the residuals and the minimum Akaike Information Criterion (AIC) were used to assess the goodness of fit of the models. After examining the results of PACF and AIC, we applied 4 *dfs* per year smoothing for time and 2 *dfs* per year each for the continuous covariates.

The following equation of the log-linear model is given below:

$$\text{Log}\,[E(y)] = \beta_0 + \beta_1 X + \beta_2 Z_1 + \beta_3 Z_2 + \Sigma\, S(\gamma_i , df_i) \quad \ldots(1)$$

E(y): Expected daily hospital admissions counts

X: pollutants concentration

Z_1: days of the week,

Z_2: holiday indicator

γ: time, temperature, rainfall, and relative humidity

β: regression coefficients

S: smoothing function using natural spline

df: degree of freedom: 2 *dfs* for temperature, relative humidity, and rainfall; 4 *dfs* per year for time

We started the modeling process by fitting the single pollutant models for each pollutant to determine the effects of the pollutants. Later we run a sensitivity analysis to measure the consistency and robustness of the estimates. The results were presented as relative risk (RR) and excess risk (ER) The ER per 10ug/m3 of each pollutant increase was calculated as ER= (RR– 1)*100. Effects of the pollutants on the current day (lag 0) to the previous five days (lag 5) were observed. We followed a similar methodology of sensitivity analysis done by Vichit-Vadakan et al. (2008) and Mahiyuddin et al. (2013).

RESULTS AND DISCUSSIONS

Descriptive Statistics

Table 1 showed the summary statistics of the hospital admissions. A total of 77,063 admissions for cardiovascular diseases and 98,869 for respiratory diseases were recorded from 1st January 2008 to 31st December 2010. There were on average, 70 admissions for cardiovascular diseases and

Table 1: Summary statistics of the daily hospital admissions (n) in Klang Valley.

Variables (n)	Mean	SD	Min	Max	Total
Cardiovascular cases	70	15.83	5	119	77063
Gender					
Male	43	10.67	13	76	47063
Female	28	7.39	11	53	30306
≥60 years old	30	7.47	8	52	33375
Respiratory cases	90	25.65	5	228	98869
Gender					
Male	50	13.92	16	114	54847
Female	41	13.44	12	119	44397
≤9 years old	87	27.27	22	234	95184

90 admissions per day for respiratory diseases. The average of male admissions was higher than females for both diseases. Forty-three percent of the cardiovascular admissions were among the 60 years old and above. Children aged less than 9 years old had the highest admissions (96%) due to respiratory diseases.

The daily average temperature in Klang Valley was 27.64°C, relative humidity 76%, and rainfall 8.65mm, indicating the tropical climate in Klang Valley. Daily average concentrations of all the pollutants were; 1066.92 $\mu g.m^{-3}$ for CO, 36.25 $\mu g.m^{-3}$ for O_3, 8.82 $\mu g.m^{-3}$ for SO_2, 42.52 $\mu g.m^{-3}$ for NO_2, and 51.40 $\mu g.m^{-3}$ for PM_{10}. (Table 2). The daily average of pollutants was compared with the ambient Malaysia air quality guideline (MAQG) in 2005 (Department of Environment 2015) together with the interim target 1 (IT-1) which was adopted by DOE in the year 2015, and WHO air quality guideline of the year 2005 (WHOAQG) (Amancio & Nascimento 2012).

The daily average of PM_{10} was 51.40 ± 15.93 $\mu g.m^{-3}$, which exceeded the WHO air quality guideline. The maximum concentration of PM_{10} was observed on 12th June 2009 with a concentration of 147.87 $\mu g.m^{-3}$ and did not exceed the MAQG 2005 and MAQG New IT-1 2015 but exceeded the WHOAQG 2005.

Fig. 2 displayed the trends of hospital admissions and air pollution concentrations together with a simple smoothing spline. Cardiovascular series showed a slightly increasing trend with seasonality fluctuations whilst respiratory series showed a clear increasing trend with a peak in 2009.

SO_2 fluctuated around a constant mean with clear seasonality with few days were found to exceed the WHOAQG 2005. NO_2 and CO declined slightly from 2008 to 2009 and started to increase in 2010 with clear seasonality. PM_{10} recorded 16 days with concentrations of more than 100 $\mu g.m^{-3}$ in 2009 which were related to the haze episodes between June to August. In contrast, O_3 showed a slight decreasing pattern from 2008 to 2010 (Fig. 3).

Modeling

Tables 3 and 4 display the significant results from the single pollutant models at various lags models. The models range from lag0 to lag5 for cardiovascular and respiratory admissions at all ages together with age and gender-specific. The highest risk for cardiovascular was found with SO_2 (RR=1.048; 95%CI: 1.007-1.091) and followed by NO_2 (RR=1.021; 95%CI: 1.009-1.033) (Table 4). Both gaseous showed an immediate or acute effect at lag0. Among the elderly, similar pollutants were found to be associated with cardiovascular admissions. Higher RR was observed among the elderly for SO_2 (RR=1.065; 95%CI: 1.012-1.120) and NO_2 (RR=1.031; 95%CI: 1.016-1.046) at lag0. However, O_3 showed a delayed effect after 2 days of exposure (RR=1.014; 95%CI: 1.003-1.026). In gender-specific analysis, higher RR was found in males compared to females. NO_2 (RR=1.025; 95%CI: 1.012-1.039) and SO_2 (RR=1.069; 95%CI: 1.019-1.120) continue to show significant associations with immediate cardiovascular admissions (lag0) for males and NO_2 for females (RR=1.018; 95%CI:1.002-1.034). Delayed effects of five days (lag5) for SO_2 (RR=1.063; 95%CI: 1.0073-1.120) and O_3 (RR=1.013; 95%CI: 1.001-1.026) were observed among females (Table 3).

In Table 4, NO_2 was the only pollutant associated with respiratory (RR=1.021; 95%CI 1.006-1.035:) at lag0. Among children less than 9 years old, NO_2 and PM_{10} were associated with respiratory admissions at similar lags which were lag0, lag1, and lag2 days. NO_2 showed the highest risk of exposure at lag0 (RR=1.031; 95%CI: 1.014-1.048) and decreasing risks were observed as the lags increased. However, a different pattern was observed in PM_{10}. Acute or immediate effect was observed at lag0 (RR=1.013;95%CI: 1.003-1.023) for PM_{10}, started to decline at lag1 (RR=1.011;95%CI: 1.001-

Table 2: Summary statistics of daily concentration of pollutants and meteorological variables in Klang Valley.

Variables	Averaging Time	Mean ± SD	Min	Max	MAQG (2005)	MAQG New IT-1(2015)	WHO AQG 2005
Temperature (°C)		27.64±1.21	23.6	30.90			
Humidity		76.06±6.57	58	93.30			
Rainfall		8.65±15.54	0.0	92.4			
CO [$\mu g.m^{-3}$]	8 h	1066.92±280.49	285.74	2363.12	10000	10000	11500
O_3 [$\mu g.m^{-3}$]	8 h	36.25±11.08	10.26	85.71	120	120	100
SO_2 [$\mu g.m^{-3}$]	24 h	8.82±2.57	2.70	33.86	105	105	20
NO_2 [$\mu g.m^{-3}$]	24 h	42.52±9.77	12.51	76.51	75	75	40
PM_{10} [$\mu g.m^{-3}$]	24 h	51.40±15.93	18.95	147.87	150	150	50

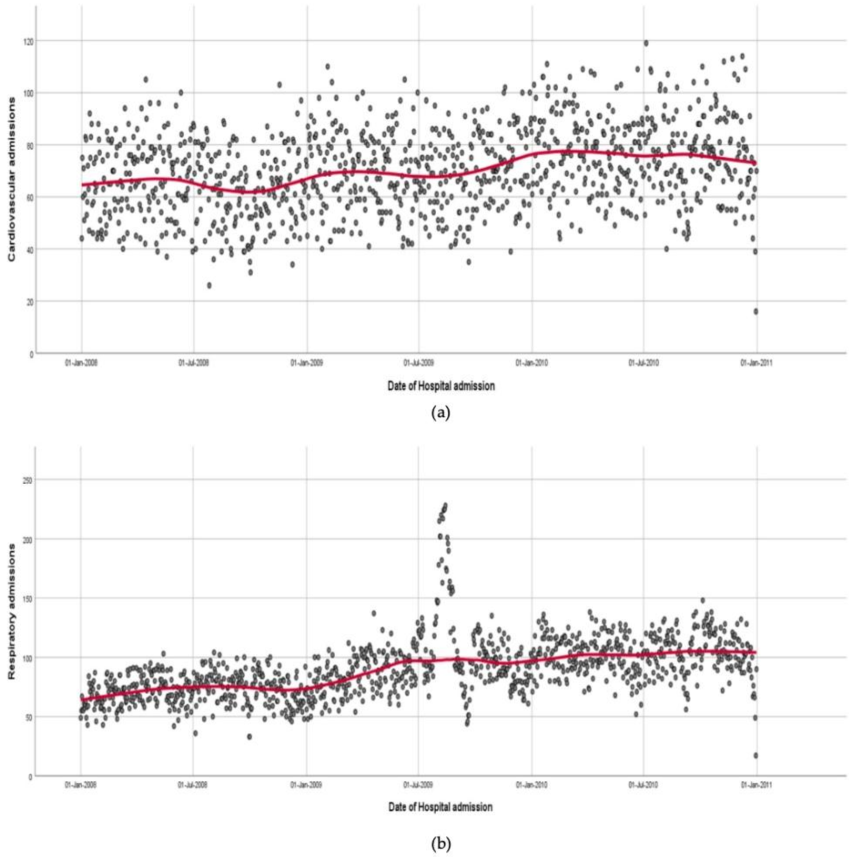

Fig. 2: The trend series of hospital admission in Klang Valley from 2008-2010.

1.021) and increased back at lag2 (RR=1.013; 95%CI: 1.003-1.022). Males continue to show higher risk compared to females. NO_2 was consistent immediately associated with males (RR=1.026;95%CI:1.012-1.041) and females (RR=1.019;95%CI: 1.001-1.037). PM_{10} was also associated with females but at various delayed effects, while CO was associated with males at immediate effect (RR=1.001; 95%CI: 1.0001-1.001).

NO_2 was chosen as the pollutant in the sensitivity analysis because it was consistently associated with cardiovascular and respiratory admissions. The sensitivity analysis was performed using alternative *dfs* for smoothing of time and

Table 3: Summary statistics of the daily cardiovascular hospital admissions (n) in Klang Valley.

Types of admissions	Pollutant	Lags	RR	Lower CI for RR	Upper CI for RR
CVD all ages	NO_2	0	1.021	1.00935	1.032641
	SO_2	0	1.048	1.007337	1.091443
CVD > 60 years old	NO_2	0	1.031	1.016239	1.046112
	SO_2	0	1.065	1.011632	1.120241
	Ozone	2	1.014	1.002755	1.026129
CVD (males)	NO_2	0	1.025	1.011795	1.039375
	SO_2	0	1.069	1.019726	1.120055
CVD (females)	NO_2	0	1.018	1.002219	1.034269
	SO_2	5	1.063	1.007391	1.120725
	Ozone	5	1.013	1.000757	1.025912

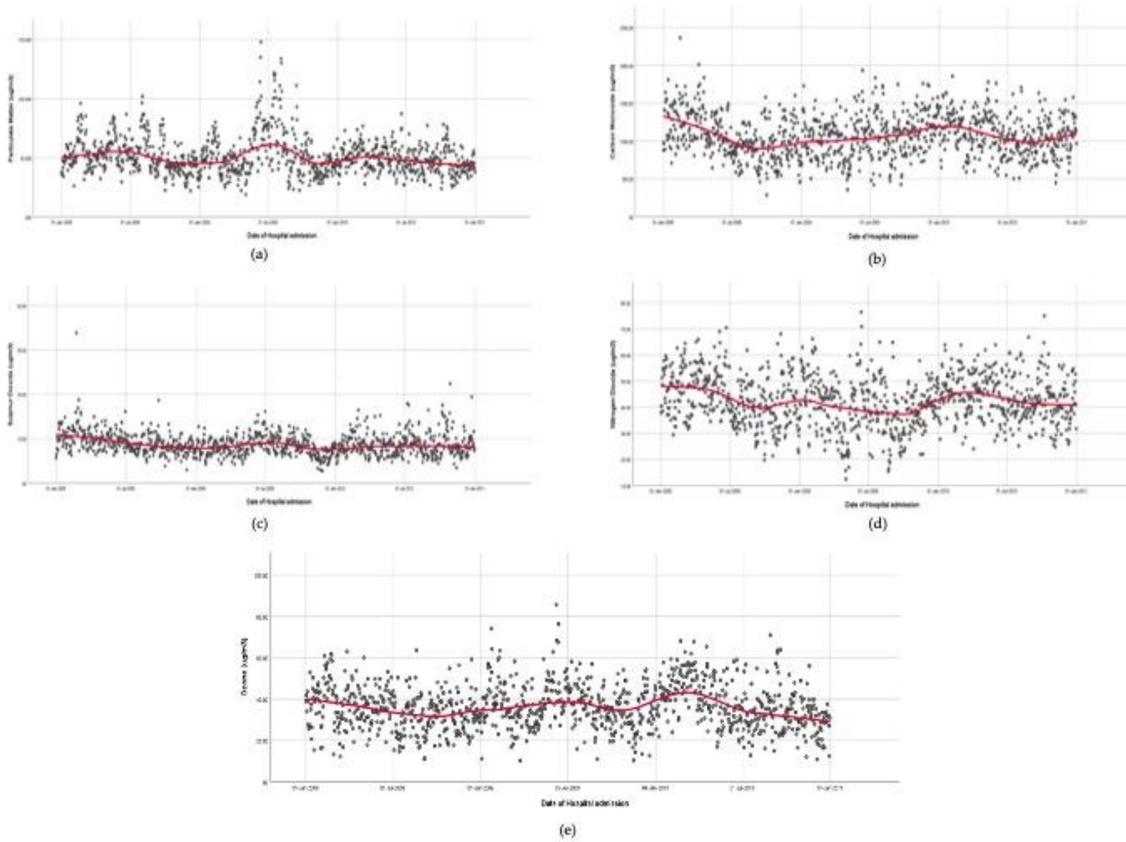

Fig. 3: Daily concentrations of pollutants in Klang Valley from 2008-2010.

Table 4**:** Summary statistics of the daily respiratory hospital admissions (n) in Klang Valley.

Types of admissions	Pollutant	Lags	RR	Lower CI for RR	Upper CI for RR
Respiratory all ages	NO_2	0	1.021	1.006467	1.035246
Respiratory < 9 years old	NO_2	0	1.031	1.013681	1.048208
		1	1.018	1.00096	1.034336
		2	1.018	1.001518	1.034099
	PM_{10}	0	1.013	1.002759	1.022943
		1	1.011	1.001228	1.020908
		2	1.013	1.002817	1.022361
Respiratory (males)	NO_2	0	1.026	1.011538	1.041365
		1	1.018	1.003517	1.032498
		5	1.015	1.011538	1.041365
	CO	0	1.001	1.000112	1.00111
Respiratory (females)	NO_2	0	1.019	1.001158	1.036559
	PM_{10}	1	1.010	1.000396	1.020393
		2	1.013	1.002749	1.022622
		3	1.013	1.002984	1.022808
		5	1.012	1.002025	1.021832

lag0. A change in the ER of >20% from the main analysis in the single pollutant model of NO_2 at various *dfs* was used to indicate the sensitivity of the data. Table 5 showed that the effects of NO_2 on cardiovascular and respiratory admissions were insensitive to the number of *df* specified. Therefore, we conclude that the effect estimates did not alter much even when we change the *df* for the smoothing of time. This suggests that the core model is relatively robust to model specification.

DISCUSSION

Our results from the study demonstrated some important findings. Three pollutants were found to exceed the WHOAQG 2005 on certain days which were SO_2, NO_2, and PM_{10}. There was an increasing trend of SO_2 in our study, with some values exceeding the WHOAQG 2005 but not exceeding MAQG 2005. The concentration of SO_2 exceeded the WHOAQG 2005 on the 23rd of February 2008 and the 28th of October 2010, with the value of 33.86 $\mu g.m^{-3}$ and 22.45 $\mu g.m^{-3}$, respectively. However, the annual average concentrations of SO_2 are still far below the WHOAQG 2005 which were less than 10 $\mu g.m^{-3}$ for the study period. As for NO_2, we found that there were in total 652 days of which the average concentrations exceeded the WHOAQG 2005 for which 230 days in the year 2008, 185 days in the year 2009, and 237 days in 2010. The number of days on which the concentrations exceeded the WHOAQG 2005 was more than 50% of the total number of days in a year.

Only gaseous pollutants were found to be associated with cardiovascular admission, which was highest in SO_2, followed by NO_2 and O_3. These associations were consistent in all types of cardiovascular admissions. Our results are consistent with the findings from Tajuddin et al. (2019) which showed a delayed effect for SO_2 at lag 4, but our study showed acute effects for SO_2 at lag0. In Thailand, Phosri et al (2019) revealed evidence of an association between SO_2 and hospital admissions with higher risks observed for cardiovascular disease. Similarly, epidemiological studies in Brazil (Amancio & Nascimento 2012) and China (Amsalu et al. 2019, Shen et al. 2020) have linked SO_2 to cardiovascular admissions and mortality, including hypertension, coronary heart disease, and stroke. The mechanisms underlying the development of circulatory disorders resulting from SO_2 exposure have not been thoroughly studied. However, the possible mechanism could be the activation of systemic vascular oxidative stress reaction (Miller 2020, Fiorito et al. 2018). Furthermore, an increase in plasma fibrinogen and inflammatory factors leads to increased blood viscosity and contributes to cardiovascular dysfunction (Peters et al. 2017).

Table 5: Summary of sensitivity analysis.

Types of admissions	*df* for time	RR	ER [%]	%Change in ER Relative to Main Analysis [%]
Cardiovascular all ages	3	1.023	2.323	11.15
	4*	1.021	2.09	
	5	1.021	2.145	2.63
	6	1.022	2.226	6.51
	7	1.024	2.448	17.13
Respiratory all ages	3	1.023	2.320	11.54
	4*	1.021	2.08	
	5	1.017	1.658	20.29[a]
	6	1.020	2.049	1.49
	7	1.023	2.259	8.61

NO_2, PM_{10}, and CO were the three pollutants that were significantly associated with respiratory admissions. We found that there were 496 days in which the concentrations of PM_{10} exceeded the concentration of WHOAQG of 50 $\mu g.m^{-3}$. The risks were higher among children less than 9 years old. NO_2 at high concentrations will highly affect those with respiratory diseases such as bronchitis and asthma (Kowalska et al. 2020, Carthy et al. 2021). Air pollution reduces the airway epithelium's defense mechanism by reducing barrier function, impairing host response against pathogens, and exaggerating inflammatory responses. The destruction of respiratory epithelium increased mucus production and bronchospasm (Huff et al. 2019).

Our study revealed that the elderly aged 60 years and above were at a higher risk for exposure to gaseous pollutants. This result is consistent with other findings from the tropical region (Yap et al. 2019, Chan et al. 2006). Chan et al. (2006) concluded that long-term exposure to NO_2, O_3, and $PM_{2.5}$ were significantly associated with increased blood pressure, total cholesterol, fasting glucose, HBA1c, IL-6, and neutrophils among elderly aged 65 years of age. However, in our study, we could not find any significant association between cardiovascular admissions with particulates, in our case PM_{10}. We found that children are also vulnerable and susceptible to air pollution. The main reason is that children's organ development, such as the lungs, does not fully develop compared to adults. Children's physiology also has a higher respiratory rate; thus, they breathe faster than adults, exposing them to higher pollutant concentrations (Zhou et al. 2019).

Among the cardiovascular admissions, both genders were susceptible to gaseous pollutants compared to particulates.

The risk for males was only slightly higher compared to females. However, females showed significant risks to particulates at various lags in respiratory admissions, which was not observed among males. Furthermore, females showed significant associations with all pollutants except CO, making females more vulnerable to pollutants compared to males. Our findings tally with other findings from all over parts of the world (Zhang et al. 2015, Boezen et al. 2005). Butter (2006) in her article explained the reasons why females are more vulnerable to air pollution. Many environmental pollutants tend to bind to the body's receptors. Receptors for estrogens and androgens in the human body modulate toxic reactions in a gender-specific way. Besides we know that males have more relative fat mass, which allows them to give a larger distribution volume for chemical particles in the environment. However, females' bodies metabolize more quickly than males, resulting in higher toxicity.

Generally, we knew that the risk of having cardiovascular disease due to air pollution is relatively small compared to the effect of established cardiovascular risk factors associated with lifestyles such as smoking, obesity, and high blood pressure. Even though the risk is small, air pollution effects are considered a severe public health problem because a large number of people are exposed over their entire lifetime.

We compare our results from this study with Mahiyuddin et al. (2013), which was done in the same urbanized area of Klang Valley. Mahiyuddin et al. (2013) observed that only PM_{10}, CO, O_3 and NO_2 were associated with mortality. However, the risks among mortality were found to be higher than the risk from this study with no acute effects at lag0 observed. This showed that the pollutants' effects on hospital admission were acute effects, which will lead to mortality after a few days of exposure.

Since the study was done in 2008-2010, we compared the concentrations of pollutants with the MAQG IT-1 for the year 2015, which was also far above the WHOAQG. Malaysia introduced the new ambient air quality standard to replace the old standard that had been used since 1989. The air pollutants concentration limit will be strengthened in stages until the year 2020. There are 3 interim targets set which include interim target 1 (IT-1) in 2015, interim target 2 (IT-2) in 2018, and the full implementation of the standard in 2020. Even with the current concentrations, the risks were still observed. Therefore, the current air quality standards might not be appropriate to protect public health in an urbanized area such as Klang Valley.

Separating the effects of one pollutant from the effects of others is often difficult. At the same time, not all members of the population are equally sensitive to such effects. Some subgroups such as the elderly, asthmatics children, and people with heart diseases are more likely to be at risk from exposure to air pollution compared to others. Several epidemiological studies have shown that the individual effects of air pollution are normally rather small. However, the public health effect can be substantial. This also means that in general, everyone in the world is exposed to air pollution, but in varying degrees.

There are several limitations of the study that should be acknowledged. We used air pollutant data from fixed-site monitoring stations, as in all other similar time series studies, rather than measuring individual exposures. This causes measurement errors in the assessment of exposure, but these errors are generally random. Second, we assumed that all individuals in the study area were equally exposed to almost the same air pollutants at all times, which may not be accurate.

CONCLUSION

This study found that NO_2, CO, and PM_{10} increased the risk of hospital admission for cardiovascular and respiratory diseases among the residents of Klang Valley, Malaysia. The elderly, children, and females have been identified as vulnerable sub-populations to air pollution. As the concerns about these health effects, regulations to reduce emissions of harmful air pollutants have been discussed and implemented at the international, regional, national, and local levels. Thus, there is a need for accurate evidence and comparable estimates between countries on the health effect of air pollution as a foundation for designing scientific and effective strategies to reduce these effects.

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