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# Association Between Particulate Matter ($PM_{10}$) Exposure and Cardiorespiratory Hospital Admissions: A Time Series Analysis

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**Abstract:** This study aimed to evaluate the association between particulate matter ($PM_{10}$) exposure and cardiorespiratory hospital admissions and develop a time series model for cardiorespiratory hospital admissions in Johor, Malaysia. Retrospective time series analysis was utilised to study cardiorespiratory hospital admissions for the study period 2015-2016. Over-dispersed Poisson generalized linear models with parametric smoothing functions were used to examine the association between cardiorespiratory admissions and $PM_{10}$ exposure. Male patients have a higher mean age at admission compared to female patients for cardiovascular admissions. Correlations were weak between $PM_{10}$ concentration and meteorological data. Time series analysis yielded insignificant results in establishing the association between $PM_{10}$ and both cardiorespiratory hospitalisations after adjusting for long-term trend, seasonal patterns and meteorological covariates. The findings from this study contribute to the heterogeneity of existing literature on this subject. More studies need to be conducted with the use of multipollutant models and adjustments for more confounding variables. The methodology used here is proposed as a way to explore reproducibility of air pollution effects on risk of cardiorespiratory hospitalisations of urban and suburban populations in Johor, Malaysia.

**Keywords:** Air Pollutants, Cardiovascular Disease, Hospital Admissions, Respiratory Disease, Time Series

## Introduction

Air pollution has emerged as one of the major global environmental health hazards in recent years. Air pollution can be described as the occurrence of foreign substances suspended in air that negatively impacts the well-being and health of individuals, which include both CVD and respiratory disease.

In Malaysia, major air pollution sources include trades, development actions, motor automobiles, power production, land clearing, open burning and forest fires (Dominici *et al*., 2000). Additionally, Malaysia also experiences an annual worsening of air quality due to many reasons, the most prominent being the transboundary haze.

The most important cause of haze is deforestation which takes place during annual dry season between June to September in lowlands of Sumatra and Kalimantan, Indonesia (Yusof *et al*., 2017). Traditionally they are set by small scale landholders for agricultural purposes. However, more recently haze is caused by major deforestation for palm oil plantations and peat fires.

Particulate Matter (PM) can penetrate deep into respiratory airways and enter the bloodstream causing respiratory, cardiovascular and cerebrovascular adverse health effects. $PM_{10}$ can indirectly lead to the development of CVD and respiratory disease by increasing oxidative stress and activation of inflammatory pathway. This is exceptionally detrimental for patients with pre-existing respiratory conditions, as PM exposure can result in acute exacerbation of their chronic disease (Fajersztajn *et al*., 2017).

The thick smoke that engulfed Southeast Asia during September-October of 2015 was possibly the worst haze episode since 1997, when land use fires caused billions of dollars in damage and thousands of premature deaths (Koplitz *et al*., 2016). With prevailing winds blowing north-eastward during the haze period, prolonged and large-scale forest fires in Sumatra and Kalimantan bring plumes from fires in Borneo to the southern regions of Malaysia, especially Johor (Hanafi *et al*., 2019).

The aim of this study is to develop a time series model for cardiorespiratory hospital admissions in Johor for the years 2015 and 2016.

## Methods

### *Study Area*

Johor was chosen as the location of the study as it is a semi-urban state in the southern part of Malaysian peninsula that is geographically near to and faces Sumatra. Johor is the second largest state located in the southern part of Peninsula Malaysia with an area of 19,166 km$^2$. In 2019, it has a population of 3.76 million with an approximate annual population growth rate of 0.4%. Johor, like the rest of Malaysia, is located near the equator and has a tropical climate. Throughout the year, both the temperature and humidity are constantly high with regular heavy rainfall. Forest fires are a concern for the state with more than 380 incidents recorded in 2016, caused by farmers clearing their land for agricultural use (Bernama, 2016).

The major development zone in Johor known as Iskandar Malaysia spans an area of 221,634 hectares. Along with this economically valuable development process, increased atmospheric pollution has also been observed as an unfortunate consequent. It was reported that commercial and industrial activities in Iskandar Malaysia had the highest contribution towards air pollutant emissions (Azahar *et al*., 2016).

### *Cardiorespiratory Hospital Admissions Data*

Three hospitals in Johor were selected for this study: Hospital Sultanah Aminah, Hospital Pakar Sultanah Fatimah and Hospital Segamat. The study population is daily cardiorespiratory hospital admissions to Ministry Of Health (MOH) facilities in Johor in 2015-2016, for patients aged above 2 years old, with a total of 47,931 admissions. The decision to omit paediatric patients aged below 2 years old is based on several research articles that reported weak correlations between respiratory admissions of patients aged 0-2 years old and $PM_{2.5}$ concentrations (Zhou *et al*., 2019).

For the first age stratum of 3-12 years old, this is the paediatric age group where children are thought to be more susceptible to higher air pollution levels than adults (Lin *et al*., 2003). For the second age group of 13-65 years of age, this population is highly active, mobile and independent. Therefore, it is more exposed to air pollution than the other two groups (Lin *et al*., 2003).

The cut-off point for the highest age stratum at 65 years old is based on previous findings where the elderly aged over 65 are the most susceptible to extreme weather conditions (Wang *et al*., 2020).

The International Classification of Disease, Tenth Revision rubrics of the health outcomes were as follows: Cardiovascular diseases (ICD-10: I00 to I99) and respiratory diseases (ICD-10: J00 to J99).

### *Air Quality Data*

These hospitals were matched to nearby Continuous Air Quality Monitoring (CAQM) stations located in Kota Tinggi, Pasir Gudang, Johor Bharu, SM Teknik Muar. Daily environmental data from four CAQM stations data ($PM_{10}$, temperature, relative humidity and rainfall) in 2015-2016 were included in the study.

### *Study Design and Statistical Analysis*

The summary statistics were performed using Microsoft Excel and statistical analyses were generated using Stata software version 16. A Generalised Additive Model (GAM) using a Poisson distribution with a log-link function was implemented to construct the principal models, adapted from Mahiyuddin *et al*. (2013). These were utilised to regress the daily number of cardiorespiratory hospital admissions as the outcome variable. The covariates include the time variable (day), daily mean $PM_{10}$ concentration, temperature, relative humidity and rainfall. This Poisson model integrated flexible spline smoothing functions to adjust for long-term trends and seasonal patterns in cardiorespiratory hospital admissions. The variables were supplemented to the principal model to control systematic differences over time, long-term annual trends and short-term temporal variations of the day of the week.

The equation below explains the Poisson regression in GAM:

$$Log\left[E(y)\right] = \beta_0 + \beta_1 Z_1 + \Sigma S(\gamma_i, df_i)$$

Where:
$E(y)$: Expected daily hospital admission counts
$Z_1$: Dummy variable - days of the week
$\gamma$: Covariates - $PM_{10}$ concentration, temperature, humidity and rainfall
$\beta$: Regression coefficients
$S$: Smoothing function using flexible spline
$df$: Degree of freedom or knots

The modelling procedure was divided into five stages: (1) Modelling short-term fluctuations, (2) modelling lag effects of exposure, (3) modelling lag effects of exposure, (4) goodness of fit testing and (5) model checking with residuals. The results are discussed in terms of Incidence Rate Ratio (IRR) and Excess Risk (ER) of CVD and respiratory hospital admissions for every 10-unit increment of the daily mean $PM_{10}$ concentration as per convention, where ER per Interquartile Range (IQR) were calculated as ER = (RR-1) ×100 (Davoodabadi *et al.*, 2019).

## Results

### *Descriptive Analysis*

Table 1 and 2 summarise patient demographics, daily hospital admission rates, $PM_{10}$ concentrations and meteorological conditions for Johor over the study period. The mean ages for CVD and respiratory admissions were 57.55±15.32 ($p<0.001$) and 41.16±27.85 ($p = 0.0013$), respectively, with 62.93% of CVD admissions and 55.42% of respiratory admissions comprising of male sex. For both years, females have a higher mean age at admission for CVD admissions, whereas for respiratory admissions, the mean ages between male and female were similar.

Total CVD hospitalisations (n = 25,751) to respiratory hospitalisations (n = 22,180) ratio was 1.16. Daily CVD hospitalisations have a higher mean compared to respiratory hospitalisations (35.25±8.37 versus 30.36±7.23). The correlation between daily $PM_{10}$ concentrations and meteorological levels were negative and not significant at the 0.05 level (temperature: -0.02, relative humidity: -0.01, rainfall: -0.06). Figure 1 illustrates the trend of $PM_{10}$ over the study period with a spike in concentration towards the end of 2015.

### *Analytical Results*

The estimated risk for $PM_{10}$ concentration was obtained for every IQR increase at different lag times up to seven days. Meteorological covariates and holiday indicator were included in the model as meteorological conditions are the primary factor causing the day-to-day variations in pollutant concentrations. We found no significant associations in the model (Table 3) between $PM_{10}$ and both CVD and respiratory hospital admissions at all lags. For CVD hospital admissions, there was a 0.01 excess risk of hospitalisation at lag 5 (IRR = 1.01, 95% CI = 1.00-1.01, p = 0.18). Meanwhile, though not significant, respiratory admissions were associated with an inverse excess risk for every 10-unit increment of the daily mean $PM_{10}$ concentration at lag 1 (IRR = 0.99, 95%CI = 0.98-1.00, %ER = -0.01, p = 0.16), lag 3 (IRR = 0.99, 95%CI = 0.98-1.00, %ER = -0.01, p = 0.26), lag 4 (IRR = 0.99, 95%CI = 0.98-1.00, %ER = -0.01, p = 0.15) and lag 5 (IRR = 0.99, 95%CI = 0.98-1.00, %ER = -0.01, p = 0.17).

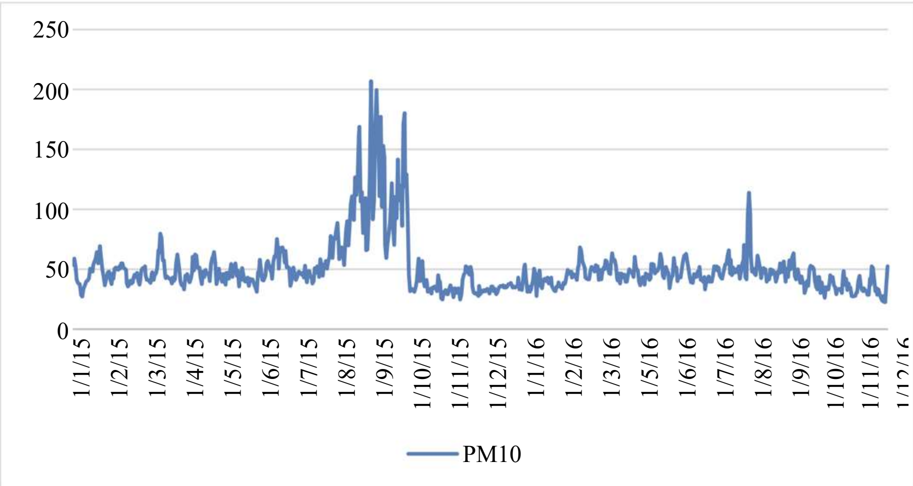


**Fig. 1:** Daily $PM_{10}$ concentrations, 2015-2016

**Table 1:** Patient Demographics of Cardiovascular and Respiratory Hospital Admissions in Johor, 2015-2016

| | | Age (mean, SD) | | | | Sex, n (%) | | |
|---|---|---|---|---|---|---|---|---|
| Disease | Age (mean, sd) | Male | Female | t-test | p-value | Male | Female | Total, n (%) |
| CVD | 57.55 (15.32) | 56.39 (14.56) | 59.51 (16.34) | -15.86 | <0.001 | 16199 (62.93) | 9544 (37.07) | 25743 (100.00) |
| Respiratory | 41.16 (27.85) | 41.70 (27.90) | 40.49 (27.77) | 3.21 | 0.0013 | 12291 (55.42) | 9887 (44.58) | 22178 (100.00) |

**Table 2:** Summary statistics $PM_{10}$ concentrations and meteorological conditions in Johor, 2015-2016

| Variables | Mean | SD | Minimum | IQR | Maximum | n |
|---|---|---|---|---|---|---|
| $PM_{10}$ (mg/m$^3$) | 50.28 | 23.61 | 22.52 | 14.07 | 206.92 | 731 |
| Temperature (°C) | 27.61 | 1.66 | 24.51 | 1.34 | 38.21 | 731 |
| Relative humidity (%) | 69.13 | 7.04 | 48.64 | 9.21 | 87.23 | 731 |
| Rainfall (mm/h) | 5.91 | 10.93 | 0.00 | 6.35 | 77.70 | 731 |

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**Table 3:** Cardiorespiratory hospital admissions in different lag structures in Johor, 2015-2016

| Type of admission | Lag | IRR for every IQR increase | Lower CI for RR | Upper CI for RR | %ER | p-value |
|---|---|---|---|---|---|---|
| CVD | 0 | 1.00 | 0.99 | 1.01 | 0.00 | 0.56 |
| | 1 | 1.00 | 0.99 | 1.02 | 0.00 | 0.56 |
| | 2 | 1.00 | 0.99 | 1.01 | 0.00 | 0.77 |
| | 3 | 1.00 | 0.99 | 1.01 | 0.00 | 0.89 |
| | 4 | 1.00 | 0.99 | 1.01 | 0.00 | 0.73 |
| | 5 | 1.01 | 1.00 | 1.01 | 0.01 | 0.18 |
| | 6 | 1.00 | 0.99 | 1.02 | 0.00 | 0.60 |
| | 7 | 1.00 | 0.99 | 1.01 | 0.00 | 0.62 |
| Respiratory | 0 | 1.00 | 0.99 | 1.01 | 0.00 | 0.56 |
| | 1 | 0.99 | 0.98 | 1.00 | -0.01 | 0.16 |
| | 2 | 1.00 | 0.99 | 1.01 | 0.00 | 0.75 |
| | 3 | 0.99 | 0.98 | 1.00 | -0.01 | 0.26 |
| | 4 | 0.99 | 0.98 | 1.00 | -0.01 | 0.15 |
| | 5 | 0.99 | 0.98 | 1.00 | -0.01 | 0.17 |
| | 6 | 1.00 | 0.99 | 1.01 | 0.00 | 0.40 |
| | 7 | 1.00 | 0.99 | 1.01 | 0.00 | 0.75 |

Note: All models included temperature, humidity, rainfall and holiday indicator

**Table 4:** Age and gender-specific IRR with 95% Confidence Interval (CI) due to $PM_{10}$ for Cardiorespiratory Hospital Admissions in Johor, 2015-2016

| | Lag 0 | | Lag 1 | | Lag 2 | | Lag 3 | | Lag 4 | | Lag 5 | | Lag 6 | | Lag 7 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | IRR | 95% CI | IRR | 95% CI | IRR | 95% CI | IRR | 95% CI | IRR | 95% CI | IRR | 95% CI | IRR | 95% CI | IRR | 95% CI |
| ***Cardiovascular Disease*** | | | | | | | | | | | | | | | | |
| Gender | | | | | | | | | | | | | | | | |
| Male | 1.00 | 0.99-1.00 | 1.00 | 0.99-1.02 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.01 | 1.00-1.02 | 1.00 | 0.99-1.02 | 1.00 | 0.99-1.01 |
| Female | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.02 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.01 | 1.00-1.02 | 1.00 | 0.99-1.02 | 1.00 | 0.99-1.01 |
| Age | | | | | | | | | | | | | | | | |
| 2-12 | 1.00 | 0.98-1.01 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.01 | 1.00-1.02 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 |
| 13-64 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.02 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.01 | 1.00-1.02 | 1.00 | 0.99-1.02 | 1.00 | 0.99-1.01 |
| ≥65 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.02 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.01 | 1.00-1.02 | 1.00 | 0.99-1.02 | 1.00 | 0.99-1.01 |
| Gender and age | | | | | | | | | | | | | | | | |
| Male 2-12 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.02 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.01 | 1.00-1.01 | 1.00 | 0.99-1.02 | 1.00 | 0.99-1.01 |
| Male 13-64 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.02 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.01 | 1.00-1.02 | 1.00 | 0.99-1.02 | 1.00 | 0.99-1.01 |
| Male ≥65 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.01 | 1.00-1.02 | 1.00 | 0.99-1.01 | 1.00 | 0.98-1.01 |
| Female 2-12 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.02 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.01 | 1.00-1.01 | 1.00 | 0.99-1.02 | 1.00 | 0.99-1.01 |
| Female 13-64 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.01 | 1.00-1.02 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 |
| Female ≥65 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.02 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 | 1.01 | 1.00-1.02 | 1.00 | 0.99-1.02 | 1.00 | 0.99-1.01 |
| ***Respiratory Disease*** | | | | | | | | | | | | | | | | |
| Gender | | | | | | | | | | | | | | | | |
| Male | 1.00 | 0.99-1.01 | 0.99 | 0.98-1.00 | 1.00 | 0.99-1.01 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 |
| Female | 1.00 | 0.99-1.00 | 0.99 | 0.98-1.00 | 1.00 | 0.99-1.01 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 |
| Age | | | | | | | | | | | | | | | | |
| 2-12 | 1.00 | 0.99-1.01 | 0.99 | 0.98-1.00 | 1.00 | 0.99-1.01 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.01 | 1.00 | 0.99-1.01 |
| 13-64 | 0.99 | 0.99-1.00 | 0.99 | 0.98-1.00 | 1.00 | 0.99-1.01 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 1.00 | 0.98-1.01 | 1.00 | 0.99-1.01 |
| ≥65 | 1.00 | 0.99-1.01 | 0.99 | 0.98-1.00 | 1.00 | 0.99-1.01 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 |
| Gender and age | | | | | | | | | | | | | | | | |
| Male 2-12 | 1.00 | 0.99-1.01 | 0.99 | 0.98-1.00 | 1.00 | 0.99-1.01 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 |
| Male 13-64 | 1.00 | 0.99-1.01 | 0.99 | 0.98-1.00 | 1.00 | 0.99-1.01 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 |
| Male ≥65 | 1.00 | 0.99-1.01 | 0.99 | 0.98-1.00 | 1.00 | 0.99-1.01 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 |
| Female 2-12 | 1.00 | 0.99-1.01 | 0.99 | 0.98-1.00 | 1.00 | 0.99-1.01 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 1.00 | 0.98-1.01 | 1.00 | 0.99-1.01 |
| Female 13-64 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 1.00 | 0.99-1.01 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 1.00 | 0.98-1.01 | 1.00 | 0.99-1.01 |
| Female ≥65 | 1.00 | 0.99-1.01 | 0.99 | 0.98-1.00 | 1.00 | 0.99-1.01 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 0.99 | 0.98-1.00 | 1.00 | 0.99-1.01 | 1.00 | 0.99-1.01 |

Note: All cells have p-value>0.005

Age and gender-specific IRR are illustrated in Table 4. Both male and female patients have an increased IRR of 1.01 (95%CI = 1.00-1.02) at lag 5 for CVD hospital admissions. Similarly, all three age groups have an increased IRR of 1.01 (95%CI = 1.00-1.02) at lag 5 for CVD hospitalisations. For all combinations of age and gender, there was an increased IRR of 1.01 (95%CI = 1.00-1.02) at lag 5.

Conversely, for respiratory disease, both male and female patients have a decreased IRR at lag 1, lag 3, lag 4 and lag 5 (IRR = 0.99, 95%CI = 0.98-1.00). For all age groups, there was a common increased IRR at lags 1, 3, 4 and 5 (IRR = 0.99, 95%CI = 0.98-1.00) with additional reduction in IRRs for age group 2-12 at lag 6 (IRR = 0.99, 95%CI = 0.98-1.01) and age group 13-64 at lag 0 (IRR = 0.99, 95%CI = 0.99-1.00). similarly, for all combinations of age and gender, there was a reduced IRR at lags 1, 3, 4 and 5 (IRR = 0.99, 95%CI = 0.98-1.01).

## Discussion

### *Main Findings*

Clinical studies of CVD have found that women with CVD are generally older than men with CVD and have a more complex expression of cardiovascular risk factors (Lee *et al.*, 2013). In addition to this, the ratio of male to female CVD patients is 1.7:1. This is in keeping with current evidence that men typically have a 2-fold higher incidence of CVD than women, but the gap in morbidity diminishes with increasing age as elderly women experience higher incidences of CVD.

Conversely for respiratory admissions, male and female patients present at a similar age to each other while the ratio of male to female patients is 1.24. A study conducted by Falagas *et al.* (2007) suggested that the higher prevalence of RTIs in males is more obvious for harmful and life-threatening infections like pneumonia, which is apparent in the larger number of respiratory admissions for male patients.

The ratio of CVD to respiratory hospital admissions for both years is 1.16, which indicates a higher rate of hospital admissions among CVD patients. Respiratory diseases such as acute exacerbations of bronchial asthma or COPD, or mild cases of RTIs may be treated and discharged in the emergency department itself (Reid *et al.*, 2000). The data included in this present study only analysed hospital admission trends, thus emergency department visits for respiratory illnesses were not captured in the dataset. Conversely, CVD oftentimes are potentially life-threatening thus warrants hospitalisation and subsequently further investigations and interventions.

It is worth noting that hospital admissions data were only obtained from three out of twelve MOH hospitals in Johor, with the complete exclusion of data from fourteen private medical institutions in Johor (JKN Johor, 2020). Diseases of the respiratory system and diseases of the circulatory system rank at number 1 (18.73%) and number 7 (6.50%) of the principal causes of hospitalisations in Malaysian private medical institutions for the year 2018 (Ministry of Health Malaysia, 2019).

The daily mean for $PM_{10}$ was below the limit of Malaysian Ambient Air Quality Standard (MAAQS) and at the upper limit of WHO's Air Quality Guideline. However, maximum $PM_{10}$ was double and quadruple of the upper limits of the MAAQS and WHO's air quality guideline respectively. The highest concentration of $PM_{10}$ was recorded in September 2015 and attributed to Indonesia's forest and peatland fires during the 2015 El Niño drought (Lee *et al.*, 2017). The negative correlations between $PM_{10}$ and two meteorological conditions (relative humidity and rainfall) are consistent with prior literature where high humidity is usually associated with rain occasions, subsequently reducing the particles due to wash-out processes atmospheric aerosols in the atmosphere (Mohamed Noor *et al.*, 2015).

This present study observed no significant lag effect of the estimates of the outcome variables, which are CVD and respiratory hospital admissions, even after adjustments for seasonal patterns, long-term trends, meteorological covariates and holiday indicator as well as controlling for age and sex, with the IRR values ranging from 0.99 to 1.01 for all lag days (lag 0 to lag 7) for both dependent variables in question. Lag structures were approximated using multivariate models controlling for confounding by seasonality and adjusting for overdispersion.

A systematic review aiming to evaluate the association between acute exposure to air pollution and hospitalisations due to acute decompensated cardiac failure reported that increases in PM10 concentration were associated with cardiac failure hospitalisation or death (0.63% per 10 μg/m3, 95%CI = 1.20-2.07) with the strongest association detected on the day of exposure at lag 0 (Shah *et al.*, 2013). In evaluating the impact of air pollution on CVD hospital admissions in Brazil, among nine municipalities included in the multi-city study, only two cities reported positive and statistically significant results for CVD hospitalisations, suggesting the existence of heterogeneity in current published literature (Gouveia *et al.*, 2017).

For respiratory hospital admissions, Medina-Ramon *et al.* (2006) studied the impact of $PM_{10}$ on hospitalisations for pneumonia and COPD in a multicity case-crossover study in the USA and they reported a 10 $\mu g/m^3$ increase in $PM_{10}$ during the summer months caused in a 1.47% (95% CI = 0.93-2.01) rise in COPD at lag 1 and a 0.84% (95% CI = 0.50-1.19) rise in RTIs at lag 0. Similarly, Peng *et al.* (2008) found non-statistically significant unadjusted 0.33% (95% CI = -0.21-0.86%) increase in respiratory hospital admissions for every 10 $\mu g/m^3$ increase in $PM_{10}$ concentrations and the association reduced to 0.26% after adjustments were made for PM2.5 levels.

Due to the limited availability of data, confounding variables were not measured, which can be classified into several categories: Patient factors and geographical factors. In time series studies looking at short-term temporal variability, several literatures agreed that patient factors such as smoking, socioeconomic status, or other lifestyle related factors are unlikely to have day-to-day variations in correlation with exposure to air pollutants (Pope III and Dockery, 2006). However, as previously discussed, ethnicity or race may or may not have a role in contributing to the confounder effect in this study. To be uniform with the general epidemiologic results, these confounders must correlate with air pollutant exposure across a range of dimensions of time and space, as well as be greater risk factors for CVD and respiratory disease compared to other diseases (Pope III and Burnett, 2007).

Another likely explanation for the statistically insignificant results yielded from this present study is the use of single pollutant as opposed to multi-pollutant models, due to limited data availability. In one of the earlier studies looking into the synergistic effects of multiple pollutants to health outcomes, Yu *et al.* (2013) reported the highest joint effect of $PM_{10}$ and $NO_2$ on emergency CVD hospitalisations when $PM_{10}$ and $NO_2$ levels were both at elevated levels. In addition to this, with more emerging evidence in the current literature, the multipollutant approach does not only encompass the evaluation of multiple air pollutants simultaneously in determining its relationship with the health outcome of interest, but rather is inclusive of the analysis of air pollutants and its source contributions, such as traffic emission and fuel oil combustion (Zanobetti *et al*., 2014).

### *Limitations*

This study is confined to one state and its air sampling stations within the period of two years therefore the results are valid only for that geographical location and generalizing the model to other areas should be interpreted with caution. These findings still can act as proxy to other urban areas in Malaysia and can be utilised as a baseline study to facilitate national studies to be conducted.

The study did not include data for emergency department visits, therefore milder cases of CVD and respiratory diseases were not captured. As hospital admissions commonly include the more critical cases, future research is required to evaluate the impacts of PM on other morbidity outcomes. Data was only available from MOH hospitals, therefore private hospital CVD and respiratory admissions were not included in this study.

It was also postulated in this present study that there were no scarcities of hospital beds during the haze episodes. This may not be true for some healthcare institutions. Thus, the admission statistics utilised in this study may undervalue the true potential of haze effects on the number of CVD and respiratory hospital admissions.

This present study included only a single pollutant, which does not consider possible additive/synergistic/ antagonistic effects of multiple pollutants or adjustments for collinearity.

## Conclusion

From this study, it was observed that there was a disproportionate number of CVD and respiratory admissions between male and female patients, where more male patients were admitted for these illnesses. Male patients have a higher mean age at admission compared to female patients for CVD, but the differences in age were not significant in respiratory admissions. Time series analysis of this present study produced results that were insignificant in establishing the association between air pollution and both CVD and respiratory hospitalisations, due to a multitude of reasons.

Further studies on the association between multipollutant exposure and various health outcomes may be useful in addressing research questions on exposure error and joint effects. Another pertinent area for future research is analysis using a more robust dataset, with the inclusion of more healthcare institutions (both MOH and private hospitals), even including emergency department visits, to allow for a more precise risk estimate of the adverse health outcome of interest. Geo-spatial mapping can also be considered in addition to temporal modelling in time series analysis, to produce a more robust model which can then be used to forecast health events in response to variations in air pollution exposure. The methodology used here is proposed as a way to explore reproducibility of air pollution effects on risk of cardiorespiratory hospitalisations of urban and suburban populations in Johor, Malaysia.

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## Authors' Contributions

**Nur Nabila Abd Rahim:**

- Study conception and design
- Analysis and interpretation of results
- Draft manuscript preparation

**Abqariyah Yahya:**

- Study conception and design
- Analysis and interpretation of results
- Review of results

**Wan Rozita Wan Mahiyuddin:**

- Data collection
- Analysis and interpretation of results
- Review of results

## Ethics

Ethical approval for this study was obtained from the Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia.

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