Heart, Lung and Circulation (2023) **32**, 79–89
1443-9506/22/$36.00
https://doi.org/10.1016/j.hlc.2022.10.009

ORIGINAL ARTICLE

Effects of Air Pollutant Exposure on Acute Myocardial Infarction

Maryam Mohammadian-Khoshnoud, MSc [a], Hossein Habibi, PhD [b], Babak Manafi, MD [c], Gholamreza Safarpour, MD [c], Ali Reza Soltanian, PhD [d,*]

[a]Department of Biostatistics, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran
[b]Department of Environment, College of Basic Sciences, Hamedan Branch, Islamic Azad University, Hamedan, Iran
[c]Department of Heart Surgery, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran
[d]Modeling of Noncommunicable Diseases Research Center, Hamadan University of Medical Sciences, Hamadan, Iran

Received 19 June 2022; received in revised form 11 October 2022; accepted 13 October 2022; online published-ahead-of-print 22 November 2022

Background Air pollution is a consequence of industrial development that is exacerbated as a result of population growth, and urbanisation.

Aim The goal of the study is to investigate the effects of air pollution on the number of cases of acute myocardial infarction (AMI) according to gender using the Zero-inflated Poisson Regression model in Hamadan, Iran.

Methods The study used an ecological design, and data collected from March 2016 to September 2020 in Hamadan were included. The intended response was the number of cases of AMI recorded in the investigated period. The time lag of the pollutants was used to investigate the effect of air pollution on the number of AMIs.

Results The number of AMI recorded for men and women was 1,195 and 553, respectively. The average age (±SD) for men and women was 64.60 (±12.27) and 70.98 (±11.79) years, respectively. According to the air quality index in Hamadan, the values of particulate matter < 2.5 μm ($PM_{2.5}$), SO_2, O_3, and CO were below moderate levels. Also, according to NO_2 and particulate matter between 25 μm–10 μm (PM_{10}), the air quality index of Hamadan was in the very unhealthy mode just for 2 and 3 days, respectively. The O_3 and NO_2 are significant positive effects on AMI among men. But, $PM_{2.5}$, PM_{10}, and SO_2 are negative impacts on hospitalisation in men due to AMI. For women, $PM_{2.5}$ and O_3 had positive effects on AMI. But, NO_2 and PM_{10} had a significant negative impact on hospitalisation in women during different time lags.

Conclusions The results of the study showed that if the analyses are based on gender, the responses to pollutants are different and hence the stratified analysis is important.

Keywords Air pollution • Acute myocardial infarction • Cardiovascular diseases • Zero-inflated model • Bayes estimator

Background

Industrial development and technological advancement have introduced various achievements for human life. However, sometimes unwanted and harmful waste is released into the environment as a result of advancement and the implementation of industrial development programs, which can have quite negative effects on the environment [1]. Air pollution is a consequence of industrial development that is exacerbated as a result of population growth, urbanisation, and the increased consumption of fossil fuels [1]. Today, air pollution in different urban centres around the world is one

*Corresponding author at: Ali Reza Soltanian, Modeling of Noncommunicable Diseases Research Center, Hamadan University of Medical Sciences, Hamadan, Iran; ORCID 0000-0002-7483-3502; Email: soltanian@umsha.ac.ir

of the major environmental issues resulting from the industrial civilisation of human beings and is considered a significant risk factor for human health [2,3]. In examining the effects of air pollution on the occurrence of diseases, two groups of pollution are considered. Outdoor pollution and indoor pollution. The aim of this study was to investigate the effect of outdoor air pollution on the number of hospitalisations of heart patients due to acute myocardial infarction (AMI); indoor air pollution was not the subject of this study. Common sources of outdoor air pollution are emissions caused by combustion processes from motor vehicles, solid fuel burning, and industry. The most common ambient air pollutants include suspended particles, ozone (O_3), nitrogen dioxide (NO_2), carbon monoxide (CO), and sulfur dioxide (SO_2). Also, air pollution is divided into primary and secondary pollutants. Primary pollutants are materials that are directly released from their sources into the air and include CO, NO_2, SO_2, particulates, and lead. Secondary pollutants are produced through the transformation made in the atmosphere, and O_3 is classified in this group [1].

Acute myocardial infarction (with code ICD10: I21.9) is myocardial necrosis that occurs as a result of acute coronary artery occlusion. Symptoms include chest discomfort with or without shortness of breath and nausea. The only way to initially treat an acute myocardial infarction is to open the blocked artery. Currently, the approved and standard method for the treatment of acute myocardial infarction is to perform angiography to identify the involved vessel and remove its blockage by removing the blood clot through angioplasty. After initial treatment and opening of the blocked vessel, patients must be hospitalised for 3 to 5 days to prevent acute complications of acute myocardial infarction. This hospitalisation was in the critical care unit (CCU) department for the first days, and after ensuring that the patient's condition is stable, the treatment can be continued outside the CCU department. The standard incidence of AMI in Iran is 73.3 per 100,000 people and it varies significantly from 24.5 to 152.5 per 100,000 people in 31 provinces of Iran. The adjusted incidence rate of AMI in Hamadan is 57.6 per 100,000 people [4].

Many risk factors are important for the development of MI, including lifestyle, environmental factors, psychosocial factors and genetic factors [5]. Recent epidemiological studies have shown that short-exposure to particulate matter <2.5 μm ($PM_{2.5}$) and NO_2 led to an increase in the risk of AMI [6,7]. Also, O_3 is an important risk factor in hospitalisation due to AMI [6]. Studies show that short-term exposure to moderate to severe air pollution is associated with an increased risk of AMI [8].

Nevertheless, the association between air pollution and AMI is still debated. Some studies have shown a correlation [9,10]; other studies have found either no correlation [11,12], or only related to selected pollutants [13,14]. Thus, the goal of the current study is to investigate the effects of air pollution (SO_2, NO_2, CO, O_3, particulate matter between 25 μm–10 μm [PM_{10}], $PM_{2.5}$) on the number of AMI according to gender using the Zero-inflated Poisson (ZIP) Regression model in Hamadan, in western Iran.

Material and Methods

The current study was approved by the Ethics Committee of Hamadan University of Medical Sciences with the code IR.UMSHA.REC.1399.459. To conduct research and evaluate its results, there are two steps:

1. Is there a relationship between exposure and the risk of disease? To achieve this goal, the following assessments are carried out:
   a. Examining group attributes: ecological research.
   b. Examining individual characteristics: case-control and cohort.
2. If there is an association, then we examine whether there is a possibility of causation.

The first step to determining the existence of a relationship is to use ecological research. This type of research can be a guide for studies that help clarify the causal relationship. If the results of ecological studies indicate the existence of a relationship, the next goal may be to design a study to investigate the relationship between the exposure and the desired response. The importance of these studies is that they can reveal relationships between individuals and society [15]. In ecological studies, the unit of analysis is populations or groups of people and measurements are population measures. In these studies, individual level exposure is not considered. One of the advantages of these studies is the generation of hypotheses for further investigation at the individual level.

Therefore, this study used an ecological design, and data collected from March 2016 to September 2020 in Hamadan were included. The AMI and pollution data were collected from Farshchian Cardiovascular Subspecialty Medical Center, and the Department of Environment in Hamadan, respectively. Farshchian cardiovascular medical research and training hospital is the only specialised cardiology hospital in Hamadan city, and where all cardiac patients in Hamadan city are referred. People who lived in Hamadan for at least 3 years until 2016 were considered for inclusion. In this study, 5-year daily data on AMI and air pollution were extracted in the form of a total population sampling. Therefore, it can be said that the obtained results can be generalised to the city of Hamadan.

The air pollutants included O_3, CO, NO_2, SO_2, PM_{10}, and $PM_{2.5}$, and the 24-hour average of these pollutants was extracted from Hamadan Environmental Organization. Also, the information of patients who were admitted to Farshchian Hospital in Hamadan due to AMI between March 2016 and September 2020 was extracted daily. In fact, for each day, data included the 24-hour average of air pollutants and the number of hospitalisations due to AMI.

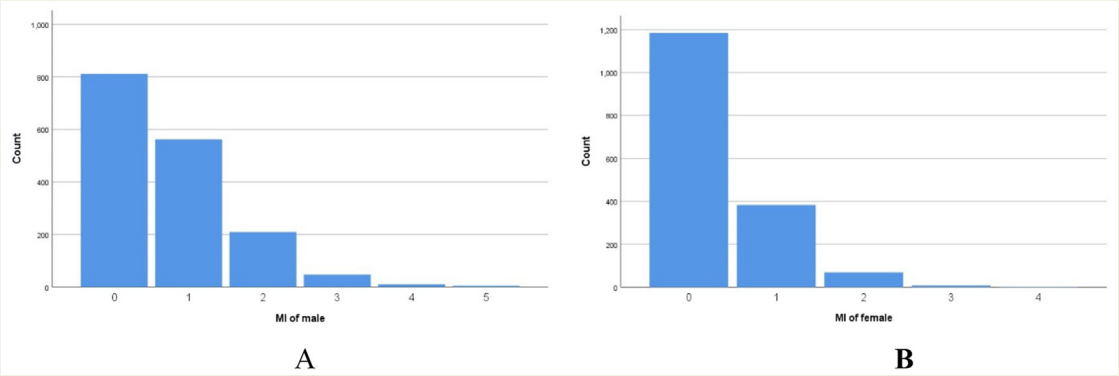

Figure 1 Frequency of the recorded severe heart attacks during 2016–2020 according to gender; A: Males, B: Females.

Hamadan Geography

Hamadan province is located in the longitude 340°47 and E360°49 and the latitude 580°33 and N480°35 in the west of Iran. It has a 3,000-year history and a population of around 1.75 million people. Its climate is semi-arid, and the annual rainfall is around 300 mm. The rains begin from October and continue until May and reach their apex in November and February. The average monthly temperature ranges between -4C° and 25C°, and the average annual temperature is 11C° [16].

Statistical Analysis

In the current study, the intended response was the number of AMI recorded. As is evident in Figure 1, the majority of responses (number of AMIs) were zero among men (49.2%) and women (71.9%). Therefore, the Vuong test was implemented to compare the Zero-inflated Poisson and the Poisson Regression models. Based on the Vuong test, it was found that the Zero-inflated Poisson Model is more fit to the data (for both men and women, $p<0.001$). Ordinary models such as the Poisson regression result in inaccurate estimates when a large number of zeros is present. Thus, the Zero-inflated Poisson Regression was used to solve this problem and make more accurate estimates. For the analysis of data, we used the Zero-inflated Poisson (ZIP) model. In the ZIP model, the y_{is} are responses and independent in the following manner [17,18]:

$y_i \sim 0$ with probability πi

$y_i \sim poisson(\lambda_i)$ with probability (1-π_i)

so that,

$$p(y_i = 0) = \pi_i + (1 - \pi_i)\, e^{-\lambda_i}$$

$$p(y_i = k) = \frac{(1-\pi_i)e^{-\lambda_i}\lambda_i^{k}}{k!} \quad K = 1, 2, \ldots$$

The independent variables related to the Poisson and logistics sections of the ZIP model can be either similar or dissimilar. If similar variables affect λ_i and π_i, and if π_i is written as a function of λ_i, then:

$$logit(\pi_i) = -\tau x'_i\beta$$

$$logit(\lambda_i) = x'_i\beta$$

Coefficients provided by the zero-inflated Poisson model were transformed into incidence risk ratio (IRR), using the Poisson regression coefficient. The variables considered in the current study included day, month, the 24-hour average of pollutants including NO_2, CO, SO_2, O_3, and particulates smaller than 2.5 and 10 microns ($PM_{2.5}$, PM_{10}). The time lag of the pollutants was used to investigate the effect of air pollution on the number of AMIs. In the current study, the effect of single-day (days 0 to 7) and cumulative lags (i.e., lag 0-7, lag 0-5, lag 0-2) were investigated. The time lag is defined as the time interval between exposure to air pollution and hospitalisation due to acute myocardial infarction. The time lag is considered because the effect of exposure to pollutants is observed not only on the same day but also days after exposure to pollution. For example, lag 2 means how much the effects of air pollution 2 days ago are on today's hospitalisation due to AMI. In the cumulative log, the effects of air pollution over the past few days on the number of hospitalisations due to AMI were investigated. For example, lag 0–2 means how much the effects of air pollution over the previous 2 days are on today's hospitalisation due to AMI.

Since the amount of pollutants had not been recorded for some days, the na.interpolation function in the R software used and the missing data were imputed using the linear interpolation argument. In addition, stratified analysis is applied to investigate the effect of air pollution on the subgroups divided according to gender. The analyses were conducted using the SPSS 26 (IBM Corp., Armonk, NY, USA) and R 4.0.2 (Foundation for Statistical Computing, Vienna, Austria) with Nonnest2, imputeTS, and Hmisc packages.

Table 1 Characteristics of air pollutants in Hamadan during March 2016 – September 2020.

Variables	Mean	SE	Minimum	Percentile			Maximum
				25%	Median	75%	
O_3 ppb	16.72	0.22	4.20	11.56	15.42	19.36	66.00
CO ppm	13.98	0.21	0.23	10.95	16.19	18.30	53.59
NO_2 ppb	53.25	1.02	1.58	15.18	44.54	84.70	259.43
SO_2 ppb	12.63	0.25	0.16	9.32	11.92	17.04	112.13
PM_{10} ug/m^3	36.71	1.20	0.42	1.30	2.17	70.26	323.41
$PM_{2.5}$ ug/m^3	24.20	0.26	3.29	16.99	22.86	29.98	90.97

Abbreviations: PM, particulate matter; ppb, parts per billion; ppm, parts per million; O_3, ozone; CO, carbon monoxide; NO_2, nitrogen dioxide; SO_2, sulfur dioxide.

Results

Statistics and Information on AMI

From March 2016 to September 2020, 1,748 AMIs had been recorded in Hamadan. The number of AMIs recorded for men and women was 1,195 and 553, respectively. The average age (±SD) for patients is 67.16 (12.42) years. The average age (±SD) for men and women was 64.60 (±12.27) and 70.98 (±11.79) years, respectively. The descriptive statistics related to air pollutants have been presented in Table 1. The maximum number of recorded daily incidences of AMI in Farshchian Cardiovascular Subspecialty Medical Center was five for men, three for women (Figure 1), and seven for total. The total average of daily AMI was 1.06, being 0.73 for men and 0.34 for women (Figure 1).

Statistics and Information on Air Pollution

During the 1,647 days that were investigated in the current study, the mean and median of CO were 13.98 ppm and 16.19 ppm, respectively. In addition, the mean and median obtained for nitrogen dioxide were 53.25 ppb and 44.54 ppb, respectively (Table 1). According to the air quality index in Hamadan, the presence of $PM_{2.5}$, SO_2, O_3, and CO was below moderate levels. The air quality index in Hamadan showed that in terms of NO_2 and PM_{10}, the air was unhealthy for 20 and 26 days, respectively. The records of meteorology stations showed that according to NO_2 and PM_{10}, the air quality index of Hamadan was in the very unhealthy mode only for 2 and 3 days, respectively.

The change pattern of air pollutants from 2016 to 2020 is shown in Figure 2. A decreasing trend can be observed in terms of O_3 (p-value=0.006), $PM_{2.5}$ (p-value=0.0005), and PM_{10} (p-value=0.0005) from 2016 to 2020, and it was found to be significant using the Cochran-Armitage test. However, the trend of change for CO (p-value=0.0005), NO_2 (p-value=0.0005), and SO_2 (p-value=0.0005) was increasing during the same period, and it was found significant using the Cochran-Armitage test.

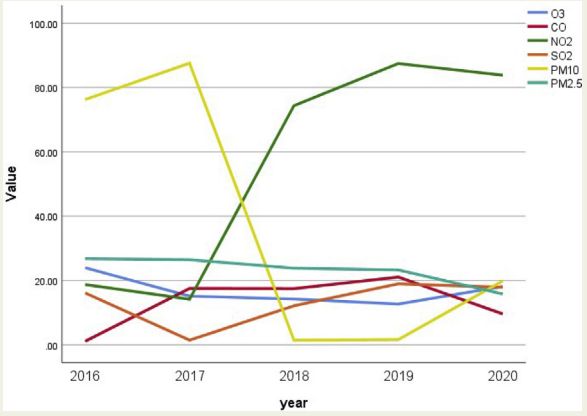

Figure 2 The trends recorded for ozone (O_3), carbon monoxide (CO), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and particulates smaller than 2.5 and 10 microns ($PM_{2.5}$, PM_{10}).
Abbreviations: AMI, acute myocardial infarction; PM, particulate matter; CO, carbon monoxide; O_3, ozone; SO_2, sulphur dioxide; NO_2, nitrogen dioxide.

Relationship Between AMI and Air Pollution

The results of fitting the Zero-inflated Poisson Regression model according to each gender and time lags were as follows:

Effects of air pollution on AMI in men

In the "count" component of the Zero-inflated Poisson model, the O_3 and NO_2 are significant positive effects on AMI among men (that is, as O_3 and NO_2 increased, so did the incidence of AMI). But, $PM_{2.5}$, PM_{10}, and SO_2 are negative impacts on hospitalisation in men due to AMI. The results of the study showed that the impact of O_3 on AMI in men occurs only 2 days before hospitalisation. A one-unit increase in O_3 increased the possibility of AMI among men by 0.09%. The effect of increased NO_2 on

Table 2 The fit of the model for AMI among men in single (0 to 7 days) and cumulative (0-2, 0-5, 0-7) lags.

	Variables	Count			Zero-Inflation		
		Beta	SE	P-value	Beta	SE	P-value
Lag 0	O_3	-0.004	0.005	0.412	-0.522	0.338	0.123
	CO	-0.011	0.006	0.064	-0.161	0.159	0.313
	NO_2	0.001	0.001	0.340	0.418	0.021	0.042*
	PM_{10}	-0.001	0.002	0.498	0.034	0.014	0.016*
	$PM_{2.5}$	0.002	0.004	0.525	-0.063	0.056	0.262
	SO_2	-0.006	0.004	0.157	-0.030	0.059	0.612
	Month	-0.004	0.011	0.678	-0.317	0.163	0.052
	Day				-0.083	0.072	0.246
Lag 1	O_3	0.002	0.004	0.642	-0.284	0.152	0.061
	CO	-0.004	0.005	0.392	0.035	0.089	0.690
	NO_2	-0.000	0.001	0.900	-0.014	0.020	0.463
	PM_{10}	-0.002	0.001	0.016*	-0.017	0.024	0.486
	$PM_{2.5}$	0.005	0.004	0.160	-0.019	0.051	0.714
	SO_2	-0.005	0.004	0.220	0.027	0.029	0.342
	Month	0.011	0.010	0.294	0.094	0.128	0.466
	Day				-0.349	0.118	0.003**
Lag 2	O_3	0.009	0.004	0.040*	0.233	0.136	0.086
	CO	0.000	0.005	0.941	0.015	0.093	0.876
	NO_2	-0.001	0.001	0.656	-0.011	0.020	0.573
	PM_{10}	-0.002	0.001	0.077	-0.118	0.076	0.120
	$PM_{2.5}$	0.001	0.004	0.848	0.055	0.054	0.302
	SO_2	0.000	0.000	0.990	0.081	0.036	0.026*
	Month	0.002	0.011	0.087	0.700	0.405	0.084
	Day				-0.224	0.092	0.015*
Lag 3	O_3	0.003	0.004	0.475	-0.240	0.146	0.101
	CO	-0.001	0.005	0.977	0.011	0.073	0.882
	NO_2	0.001	0.001	0.909	-0.006	0.012	0.591
	PM_{10}	-0.001	0.001	0.196	-0.010	0.016	0.535
	$PM_{2.5}$	-0.005	0.004	0.230	0.009	0.041	0.825
	SO_2	-0.004	0.004	0.320	0.013	0.025	0.601
	Month	0.018	0.011	0.085	0.157	0.149	0.293
	Day				-0.246	0.094	0.009**
Lag 4	O_3	0.002	0.004	0.629	-0.275	0.138	0.046*
	CO	-0.001	0.005	0.908	-0.032	0.075	0.669
	NO_2	0.001	0.001	0.578	0.002	0.011	0.843
	PM_{10}	-0.001	0.001	0.697	-0.009	0.013	0.457
	$PM_{2.5}$	-0.006	0.004	0.094	0.024	0.039	0.544
	SO_2	-0.003	0.004	0.510	-0.002	0.026	0.939
	Month	0.014	0.010	0.188	0.077	0.156	0.623
	Day				-0.323	0.143	0.024*
Lag 5	O_3	0.005	0.004	0.237	0.547	0.273	0.045*
	CO	-0.007	0.005	0.146	-0.830	0.449	0.064
	NO_2	0.003	0.001	0.005**	0.225	0.107	0.036*
	PM_{10}	0.001	0.001	0.159	0.097	0.048	0.045*
	$PM_{2.5}$	-0.011	0.004	0.005**	-0.670	0.340	0.049*
	SO_2	-0.006	0.004	0.108	0.059	0.069	0.395
	Month	0.012	0.010	0.227	1.606	0.881	0.068
	Day				0.853	0.358	0.017*

Table 2. (continued).

	Variables	Count			Zero-Inflation		
		Beta	SE	P-value	Beta	SE	P-value
Lag 6	O_3	0.005	0.004	0.244	-0.199	0.155	0.200
	CO	-0.003	0.005	0.608	0.089	0.071	0.209
	NO_2	0.002	0.001	0.050*	-0.011	0.015	0.472
	PM_{10}	-0.001	0.001	0.334	-0.010	0.015	0.516
	$PM_{2.5}$	-0.002	0.004	0.665	0.016	0.050	0.749
	SO_2	-0.009	0.005	0.040*	0.011	0.046	0.820
	Month	0.021	0.011	0.053	0.183	0.221	0.408
	Day				-0.251	0.097	0.009**
Lag 7	O_3	0.005	0.004	0.213	11.629	9.618	0.227
	CO	-0.009	0.005	0.063	-8.368	8.299	0.313
	NO_2	0.004	0.001	0.000***	4.587	3.822	0.230
	PM_{10}	0.001	0.001	0.150	2.870	2.378	0.227
	$PM_{2.5}$	-0.010	0.004	0.006**	-8.105	6.668	0.224
	SO_2	-0.008	0.004	0.051	2.745	2.324	0.237
	Month	0.012	0.010	0.222	27.791	23.423	0.235
	Day				11.226	9.408	0.233
Lag 0-2	O_3	0.001	0.005	0.757	-0.379	0.190	0.046*
	CO	-0.004	0.005	0.466	-0.032	0.069	0.647
	NO_2	-0.001	0.001	0.557	-0.003	0.016	0.827
	PM_{10}	-0.003	0.001	0.010*	-0.002	0.014	0.883
	$PM_{2.5}$	0.004	0.004	0.283	-0.016	0.043	0.708
	SO_2	-0.004	0.004	0.319	0.012	0.035	0.746
	Month	0.014	0.010	0.169	0.084	0.113	0.453
	Day	-0.005	0.004	0.184	-0.277	0.081	0.0005***
Lag 0-5	O_3	0.005	0.005	0.300	0.407	0.162	0.012*
	CO	-0.005	0.005	0.347	0.543	0.255	0.034*
	NO_2	0.002	0.001	0.119	0.095	0.039	0.015*
	PM_{10}	0.001	0.001	0.782	0.202	0.085	0.018*
	$PM_{2.5}$	-0.009	0.005	0.051	-0.606	0.278	0.029*
	SO_2	-0.006	0.005	0.222	0.270	0.115	0.019*
	Month	0.011	0.010	0.285	0.676	0.424	0.110
	Day	0.005	0.003	0.125	0.604	0.232	0.009**
Lag 0-7	O_3	0.006	0.005	0.231	0.384	0.142	0.007**
	CO	-0.008	0.006	0.136	0.372	0.191	0.052
	NO_2	0.004	0.001	0.011*	0.116	0.054	0.032*
	PM_{10}	0.001	0.001	0.431	0.171	0.073	0.020*
	$PM_{2.5}$	-0.012	0.005	0.017*	-0.498	0.236	0.035*
	SO_2	-0.008	0.005	0.109	0.295	0.161	0.067
	Month	0.013	0.010	0.199	0.004	0.769	0.996
	Day	0.005	0.003	0.145	0.531	0.185	0.004**

Table 2 shows the fitting results of the zero-inflated Poisson regression model for men. The results of this model include two parts, zero-inflated and count. Each model is fitted in single lags (0,1,2,3,4,5,6,7) and cumulative lags 0-2, 0-5, 0-7. Lag 0 means how much the effect of exposure to pollution on the same day on the number of AMI. A time lag of 0-2 means how much the effect of exposure to air pollution from the previous 2 days before a day affects the number of AMI on that day.

Abbreviations: AMI, acute myocardial infarction; PM, particulate matter; CO, carbon monoxide; O_3, ozone; SO_2, sulfur dioxide; NO_2, nitrogen dioxide.

*Significant at the level of 0.05.

**Significant at the level of 0.01.

***Significant at the level of 0.001.

Table 3 The fit of the model for AMI among women in single (0 to 7 days) and cumulative (0-2, 0-5, 0-7) lags.

	Variables	Count			Zero-Inflation		
		Beta	SE	P-value	Beta	SE	P-value
Lag 0	O_3	-0.000	0.006	0.983	-19.457	26.952	0.470
	CO	-0.006	0.007	0.410	-107.615	123.958	0.358
	NO_2	-0.002	0.002	0.307	2.842	4.000	0.477
	PM_{10}	-0.002	0.001	0.202	-1.752	2.860	0.540
	$PM_{2.5}$	0.006	0.005	0.217	16.768	25.993	0.519
	SO_2	0.002	0.005	0.663	0.383	0.804	0.634
	Month	-0.000	0.014	0.970	-5.967	12.422	0.631
	Day				-10.499	16.747	0.531
Lag 1	O_3	-0.005	0.007	0.492	-0.344	0.183	0.060
	CO	-0.005	0.008	0.501	-0.070	0.088	0.422
	NO_2	-0.005	0.002	0.007**	-0.133	0.068	0.052
	PM_{10}	-0.004	0.002	0.009**	-0.031	0.026	0.226
	$PM_{2.5}$	0.008	0.005	0.124	0.083	0.062	0.179
	SO_2	0.003	0.005	0.637	0.059	0.045	0.192
	Month	-0.011	0.018	0.499	-0.454	0.225	0.043*
	Day				-0.077	0.067	0.251
Lag 2	O_3	0.003	0.006	0.591	-29.194	6161.98	0.996
	CO	-0.005	0.007	0.470	-28.361	6948.885	0.997
	NO_2	-0.006	0.002	0.000***	-14.864	3431.088	0.997
	PM_{10}	-0.006	0.002	0.000***	-8.495	1770.566	0.996
	$PM_{2.5}$	0.015	0.005	0.004**	25.122	4938.677	0.996
	SO_2	0.001	0.005	0.769	3.353	909.400	0.997
	Month	0.005	0.014	0.717	41.827	10115.550	0.997
	Day				3.760	39.328	0.924
Lag 3	O_3	0.013	0.006	0.027*	5.618	4.886	0.250
	CO	0.004	0.007	0.558	-11.337	10.820	0.295
	NO_2	-0.005	0.002	0.002**	-1.910	1.824	0.295
	PM_{10}	-0.004	0.002	0.010*	-0.627	0.575	0.275
	$PM_{2.5}$	0.011	0.006	0.047*	7.333	6.534	0.262
	SO_2	0.006	0.005	0.165	-8.315	8.231	0.312
	Month	0.010	0.015	0.483	25.614	23.375	0.252
	Day				-7.458	6.757	0.270
Lag 4	O_3	0.010	0.007	0.169	0.066	0.084	0.432
	CO	0.001	0.009	0.967	-0.086	0.069	0.213
	NO_2	-0.004	0.002	0.052	-0.023	0.026	0.378
	PM_{10}	-0.003	0.002	0.111	-0.014	0.011	0.225
	$PM_{2.5}$	0.008	0.007	0.255	0.115	0.074	0.124
	SO_2	0.004	0.005	0.397	-0.044	0.062	0.471
	Month	0.014	0.018	0.430	0.283	0.327	0.387
	Day				-0.160	0.197	0.418
Lag 5	O_3	0.009	0.007	0.215	0.043	0.052	0.409
	CO	0.001	0.008	0.888	-0.116	0.079	0.142
	NO_2	-0.005	0.002	0.014*	-0.007	0.016	0.672
	PM_{10}	-0.005	0.002	0.006**	-0.024	0.022	0.284
	$PM_{2.5}$	0.012	0.008	0.152	0.093	0.046	0.042*
	SO_2	0.001	0.005	0.919	-0.119	0.100	0.234
	Month	0.014	0.018	0.431	0.255	0.240	0.289
	Day				-0.178	0.160	0.267

Table 3. (continued).

	Variables	Count			Zero-Inflation		
		Beta	SE	P-value	Beta	SE	P-value
Lag 6	O_3	0.010	0.006	0.080	6.029	12.417	0.627
	CO	0.005	0.007	0.453	2.101	10.974	0.848
	NO_2	-0.005	0.002	0.004**	-2.443	5.305	0.645
	PM_{10}	-0.004	0.002	0.016*	-1.690	2.535	0.505
	$PM_{2.5}$	0.004	0.005	0.454	2.308	4.524	0.610
	SO_2	0.003	0.005	0.509	-6.407	34.731	0.854
	Month	0.010	0.014	0.450	13.196	20.431	0.518
	Day				-26.047	48.969	0.595
Lag 7	O_3	0.010	0.006	0.078	4.320	85.349	0.960
	CO	0.002	0.007	0.797	-6.601	125.530	0.958
	NO_2	-0.003	0.002	0.081	-0.706	35.084	0.984
	PM_{10}	-0.003	0.002	0.033*	-1.384	35.744	0.969
	$PM_{2.5}$	0.010	0.005	0.074	6.616	144.265	0.963
	SO_2	-0.001	0.005	0.872	-3.960	73.673	0.957
	Month	0.009	0.015	0.549	15.215	304.484	0.960
	Day				-14.730	293.864	0.960
Lag 0-2	O_3	0.011	0.006	0.076	9.972	9.149	0.276
	CO	-0.001	0.007	0.901	-29.336	27.542	0.287
	NO_2	-0.003	0.002	0.070	3.918	3.588	0.275
	PM_{10}	-0.004	0.002	0.034*	1.015	0.983	0.302
	$PM_{2.5}$	0.009	0.006	0.118	4.400	4.198	0.295
	SO_2	0.001	0.005	0.800	-38.892	36.403	0.285
	Month	0.010	0.015	0.498	39.190	36.195	0.279
	Day	0.003	0.005	0.526	-9.064	8.433	0.282
Lag 0-5	O_3	0.012	0.006	0.068	8.780	100.990	0.931
	CO	-0.001	0.008	0.960	-31.758	439.755	0.942
	NO_2	-0.007	0.002	0.002**	-6.483	46.945	0.890
	PM_{10}	-0.006	0.002	0.001***	-8.056	78.899	0.919
	$PM_{2.5}$	0.015	0.007	0.029*	40.785	383.318	0.915
	SO_2	0.003	0.005	0.525	-4.908	328.541	0.988
	Month	0.010	0.015	0.519	32.183	398.750	0.936
	Day	0.002	0.005	0.735	-19.156	197.507	0.923
Lag 0-7	O_3	0.009	0.006	0.153	12.015	135.721	0.929
	CO	0.001	0.008	0.956	-20.141	264.689	0.939
	NO_2	-0.007	0.002	0.001**	-4.857	35.988	0.893
	PM_{10}	-0.006	0.002	0.001**	-9.139	93.514	0.922
	$PM_{2.5}$	0.011	0.007	0.129	27.535	314.104	0.930
	SO_2	0.004	0.006	0.495	-3.707	52.856	0.944
	Month	0.014	0.015	0.361	58.291	755.424	0.938
	Day	0.001	0.005	0.881	-21.049	133.635	0.875

Abbreviations: AMI, acute myocardial infarction; PM, particulate matter; CO, carbon monoxide; O_3, ozone; SO_2, sulfur dioxide; NO_2, nitrogen dioxide.
*Significant at the level of 0.05.
**Significant at the level of 0.01.
***Significant at the level of 0.001.

AMI in men appeared after 5 days. This result can be seen in single (5, 6, 7) and cumulative (0-7) time lags (Table 2). $PM_{2.5}$, PM_{10}, and SO_2 have a negative impact on AMI in men. It means that a one-unit increase of $PM_{2.5}$ or PM_{10} or SO_2 decreased the possibility of AMI among men.

Effects of air pollution on AMI in women

For women, $PM_{2.5}$ and O_3 had "positive" effects on AMI (i.e., as $PM_{2.5}$ and O_3 increased, so did AMI) (Table 3). But, NO_2 and PM_{10} had a significant negative impact on hospitalisation in women during different time lags. PM_{10} and NO_2 have the greatest negative impact on hospitalisation in women due to

AMI in lag time 2 day. A one-unit increase in PM_{10} or NO_2 decreased the possibility of AMI women by about 0.06% (IRR=0.994). $PM_{2.5}$ and O_3 have the greatest impact on hospitalisation in women due to AMI in lag times 2 and 3.

The fit of the Poisson regression model with the zero-inflated regression model was compared using the Vuong test. Vuong's test showed the goodness of fit of a zero-inflated regression model. This test shows the validity and reliability of the model. Also, the information in Tables 2 and 3 has been fitted to check the validity of the model results. In this study, 5-year daily data on AMI and air pollution were extracted in the form of a total population sampling. Therefore, it can be said that the obtained results can be generalised to the city of Hamadan.

Discussion

The goal of this study was to investigate the effects of air pollutants on the number of AMI among men and women. In the current study, only outdoor pollution was taken into consideration. The results of the study show that the effects of pollutants on the incidence of AMI are different between men and women.

Ozone has a positive effect on hospitalisations due to AMI in men and women. With increasing amount of ozone, the number of hospitalisations due to AMI increases. PM_{10} has an inverse relationship with hospitalisation due to AMI in both genders. In other words, the higher the PM_{10}, the less the hospitalisation of patients. The effect of $PM_{2.5}$ is positive in women and negative in men, and the effect of NO_2 is negative in women and positive in men. SO_2 has a significant negative effect on the hospitalisation of men only in time lag 6. The effect of CO is not significant in any of the time lags.

The impact of ozone on AMI was found to be significant in both genders. The amount of ozone within 3 days before hospitalisation was found to have a significant impact on women's and men's AMI. In the study by Ruidavets, the short-term exposure to O_3 within 1-2 days before hospitalisation was found to have a significant impact on the incidence of AMI among middle-aged people without any record of cardiac illness [19].

The source of tropospheric ozone is involving photochemical reactions oxides of nitrogen (NO_x) which often contain NO_2 and NO and volatile organic compounds (VOCs). In the absence or low concentration of VOCs or CO, ozone reaches steady-state concentration depending on the intensity of sunlight, air temperature, and the ratio of NO_2 to NO concentration. In these conditions, a NO_2 molecule is converted to an O_3 molecule and a NO molecule [20]. The half-life of ozone at 20°C temperature is 3 days [21]. In this study, the effect of ozone during the 3 days on AMI was effective in both genders and after 3 days its effect disappeared.

The effect of exposure to NO_2 on the number of hospitalisation of men and women due to AMI was different. The effect of NO_2 on men's hospitalisation was positive and become evident in a few days. In a meta-analysis conducted by Mustafic, the impact of NO_2 on myocardial infarction was found to be positive [22]. Increasing the amount of NO_2 increases the number of daily myocardial infarctions on men.

But, NO_2 was negatively associated with daily AMI admissions in women. In the study conducted by Yongquan, increasing NO_2 10 mg/m^3 was found to have a significant impact on MI during lags 4, 0–5, and 0–6 [7]. Findings in the current study and the study by Yongquan showed that NO_2 has a protective impact on the number of daily myocardial infarctions. Increasing the amount of NO_2 reduces the number of daily myocardial infarctions.

Increasing PM_{10} has shown to have a significant negative impact on the number of women and men's AMI. This negative effect in women lasts up to a week, but in men, it exists only in the early days and then the effect disappears.

The findings of the study by Yongquan indicated the significant negative impact of PM_{10} on an AMI in 0–2 cumulative lag. In this study and the study by Yongquan, it was observed that increasing PM_{10} reduced the number of hospitalisation due to AMI.

Increasing $PM_{2.5}$ within 2 and 3 days before hospitalisation showed a significant positive impact on women's hospitalisation. The results of a meta-analysis conducted on 34 studies in 2012 showed the significant positive impact of $PM_{2.5}$ on MI [22]. In addition, the study by Wang showed a significant positive relationship between $PM_{2.5}$ and MI [8]. In our study, increasing $PM_{2.5}$ increases the rate of women's hospitalisation due to AMI. But, $PM_{2.5}$ was negatively associated with daily AMI admissions on men in lag 5 and lag 7 days. The study by Liao showed that between 1-year mean $PM_{2.5}$ exposure and an increase in the risk of AMI was not observed significant association.

The significant negative impact of SO_2 on the number of AMI in men was evident, but the impact of SO_2 on women's AMI was not significant. The estimation of risk in the study conducted by Yongquan indicated the protective effect of SO_2 on MI in lags 4, 0–5, 0–6, and 0–7 [7]. The relation between SO_2 and MI was found to be protective in the study by Wang, which is not significant [8].

The impact of CO on men's and women's AMI was not significant. The results of the Bhaskaran study showed little evidence of the harmful effects of dioxide on AMI. Indeed, a protective effect of CO on AMI was observed over 1–72 hours.

Perhaps the protective impact of the pollutants on the rate of AMI is ignoring the confounding variables. They are variables that inverse or nullify the relation between AMI and air pollutants.

Several possible mechanisms have been proposed for the relation between pollutants and AMI. The first potential mechanism is inflammation [23,24]. Studies have shown that exposure to air pollution increases the level of inflammatory markers such as the c-reactive protein [25]. The second mechanism is the unnatural regulation of the cardiac autonomic system [23]. Several observational studies have reported the relation between high levels of air pollution and

increased heart rate, and reduced variability of the heart rate [26,27]. The next mechanism is the increased viscosity of blood due to air pollution [28]. This can enhance the formation of thrombosis [29], accelerate atherosclerosis, and weaken the stability of atherosclerotic plaques [22]. In the fourth mechanism, air pollutants may increase the rate of vasoconstriction in cases such as endothelin [30]. In addition, mechanisms such as the direct induction of cardiac ischaemia are elicited by vasospasm or direct arrhythmogenesis [31]. Of course, these findings have been obtained in studies conducted on women [22]. All these findings obtained in experimental studies support the hypothesis that exposure to air pollution may increase the rate of myocardial infarction (MI) through several mechanisms [22].

Based on the previous studies, increased rate of inflammatory markers and heartbeat, reduced heart variability, discharge of implanted cardioverter defibrillator, changes in homeostasis, inappropriate clot formation, defect in clot formation impact of air pollutants including SO_2, NO_2, O_3, PM_{10}, $PM_{2.5}$ on increase the rate of ST-elevation myocardial infarction (STMI) [32]. Also, it seems that air pollutants, particularly $PM_{2.5}$, enhance the activity of platelets and fibrinogens, reduce the rate of endogenous thrombolysis, and stimulate the formation of platelets [33].

Limitations of the study included lack of access to information regarding the humidity and temperature of Hamadan, missing data for some days within the scope of the study, and lack of clinical information on the patients experiencing AMI. In ecological studies, comparisons and tests are not at the individual level, so the effect of some confounders cannot be controlled at the individual level. Of course, it is not necessary. Also, these types of studies can be a guide to conduct investigations that will help to clarify the causal relationship, but alone cannot determine the cause of the disease.

Recommendations

The results of the study can help to better identify the effect of air pollutants on human cardiovascular health and to try to eliminate or reduce the sources of production of these pollutants. It is also suggested the relationship between air pollution and AMI should be investigated in different cities with different levels of pollution.

Conclusion

Based on the obtained results in the current study, the impact of ozone on AMI was found to be significant and positive for both genders. The effects of $PM_{2.5}$ in women and NO_2 in men were found to be significant and positive, and this meant that they are among the risk factors for severe AMI in Hamadan. In the addition, the effects of SO_2 and CO in men were found to be negative, while the impact of PM_{10} was found to be negative in both genders. This implied the protective effects of these pollutants against AMI.

The results of the study showed that if the analyses are based on gender, the responses to pollutants are different and hence the stratified analysis is important.

Sources of Funding

None.

Disclosure Statement

No potential conflict of interest was reported by the authors.

Acknowledgments

We would like to appreciate the Vice-Chancellor for Research and Technology of the Hamadan University of Medical Sciences for supporting this work.

References

[1] Mostafavi S, Safikhani H, Zamani J. Experimental investigation of air pollution in saveh city and presenting the related solutions to reduce it. Modares Mechanical Engineering. 2019;19(12):2999–3005.
[2] Glinianaia SV, Rankin J, Bell R, Pless-Mulloli T, Howel D. Particulate air pollution and fetal health: a systematic review of the epidemiologic evidence. Epidemiology. 2004;15(1):36–45.
[3] Šrám R, Binková B, Dejmek J, Bobak M. Ambient air pollution and pregnancy outcomes: a review of the literature. Environ Health Perspect. 2005;113(4):375–82.
[4] Ahmadi A, Soori H, Mehrabi Y, Etemad K, Samavat T, Khaledifar A. Incidence of acute myocardial infarction in Islamic Republic of Iran: a study using national registry data in 2012. Eastern Mediterr Health J. 2015;21(1):5–12.
[5] Zhan C, Shi M, Wu R, He H, Liu X, Shen B. MIRKB: a myocardial infarction risk knowledge base. Database. 2019;2019:1–9.
[6] Sadeghi M, Ahmadi A, Baradaran A, Masoudipoor N, Frouzandeh S. Modeling of the relationship between the environmental air pollution, clinical risk factors, and hospital mortality due to myocardial infarction in Isfahan, Iran. J Res Med Sci. 2015;20(8):757–62.
[7] Yu Y, Yao S, Dong H. Short-term effects of ambient air pollutants and myocardial infarction in Changzhou, China. Environ Sci Pollut Res Int. 2018;25:22285–93.
[8] Wang X, Zhang X, Zhuang S, Luo Y, Kang S, Liu Y. Short-term effects of air pollution on acute myocardial infarctions in Shanghai, China, 2013-2014. J Geriatr Cardiol. 2016;13(2):132–7.
[9] Braga A, Zanobetti A, Schwartz J. The lag structure between particulate air pollution and respiratory and cardiovascular deaths in 10 US cities. J Occup Environ Med. 2001;43(11):927–33.
[10] Koken P, Piver W, Ye F, Elixhauser A, Olsen L, Portier C. Temperature, air pollution, and hospitalization for cardiovascular diseases among elderly people in Denver. Environ Health Perspect. 2003;111(10):1312–7.
[11] Barnett A, Williams G, Schwartz J, Best T, Neller A, Petroeschevsky A, et al. The effects of air pollution on hospitalizations for cardiovascular disease in elderly people in Australian and New Zealand cities. Environ Health Perspect. 2006;114(7):1018–23.
[12] Berglind N, Ljungman P, Möller J, Hallqvist J, Nyberg F, Rosenqvist M, et al. Air pollution exposure—a trigger for myocardial infarction? Int J Environ Res Public Health. 2010;7(4):1486–99.
[13] Cendon S, Pereira L, Braga A, Conceição G, Cury Junior A, Romaldini H, et al. Air pollution effects on myocardial infarction. Rev Saude Publica. 2006;40(3):414–9.
[14] Linn W, Szlachcic Y, Gong JH, Kinney P, Berhane K. Air pollution and daily hospital admissions in metropolitan Los Angeles. Environ Health Perspect. 2000;108(5):427–34.
[15] Gordis L. Epidemiology. Elsevier Health Sciences; 2013.
[16] Jalali M, Khanlari Z. Environmental contamination of Zn, Cd, Ni, Cu, and Pb from industrial areas in Hamadan Province, western Iran. Environ Geol. 2008;55:1537–43.

[17] Hedeker D, Gibbons R. Longitudinal data analysis. John Wiley & Sons; 2006.
[18] Lambert D. Zero-Inflated poisson regression, with an application to defects in manufacturing. Technometrics. 1992;34(1):1–4.
[19] Ruidavets J, Cournot M, Cassadou S, Giroux M, Meybeck M, Ferrières J. Ozone air pollution is associated with acute myocardial infarction. Circulation. 2005;111(5):563–9.
[20] Zhang J, Wei Y, Fang Z. Ozone pollution: a major health hazard worldwide. Front Immunol. 2019;10:1–10.
[21] Miller F, Silva C, Brandão T. A review on ozone-based treatments for fruit and vegetables preservation. Food Engineering Reviews. 2013;5(2):77–106.
[22] Mustafić H, Jabre P, Caussin C, Murad M, Escolano S, Tafflet M, et al. Main air pollutants and myocardial infarction: a systematic review and meta-analysis. JAMA. 2012;307(7):713–21.
[23] Ayres J. Cardiovascular disease and air pollution: a report by the Committee on the Medical Effects of Air Pollutants. Available from: http://www.advisorybodies.doh.gov.uk/comeap/statementsreports/CardioDisease.pdf.
[24] Pope Cr, Hansen M, Long R, Nielsen K, Eatough D, Wilson W, et al. Ambient particulate air pollution, heart rate variability, and blood markers of inflammation in a panel of elderly subjects. Environ Health Perspect. 2004;112(3):339–45.
[25] Bräuner E, Møller P, Barregard L, Dragsted L, Glasius M, Wåhlin P, et al. Exposure to ambient concentrations of particulate air pollution does not influence vascular function or inflammatory pathways in young healthy individuals. Part Fibre Toxicol. 2008;5(1):1–9.
[26] Pope Cr, Hansen M, Long R, Nielsen K, Eatough D, Wilson W, et al. Ambient particulate air pollution, heart rate variability, and blood markers of inflammation in a panel of elderly subjects. Environ Health Perspect. 2001;112(3):339–45.
[27] Pope Cr, Verrier R, Lovett E, Larson A, Raizenne M, Kanner R, et al. Heart rate variability associated with particulate air pollution. Am Heart J. 1999;138(5):890–9.
[28] Peters A, Döring A, Wichmann H, Koenig W. Increased plasma viscosity during an air pollution episode: a link to mortality? Lancet. 1997;349(9056):1582–7.
[29] Lucking A, Lundback M, Mills N, Faratian D, Barath S, Pourazar J, et al. Diesel exhaust inhalation increases thrombus formation in man. Eur Heart J. 2008;29(24):3043–51.
[30] Bouthillier L, Vincent R, Goegan P, Adamson I, Bjarnason S, Stewart M, et al. Acute effects of inhaled urban particles and ozone: lung morphology, macrophage activity, and plasma endothelin-1. Am J Pathol. 1998;153(6):1873–84.
[31] Liao D, Whitsel E, Duan Y, Lin H, Quibrera P, Smith R, et al. Ambient particulate air pollution and ectopy–the environmental epidemiology of arrhythmogenesis in Women's Health Initiative Study, 1999-2004. J Toxicol Environ Health A. 2009;72(1):30–8.
[32] Shahrbaf M, Mahjoob M, Khahesh l, Akbarzadeh M, Barkhordari E, Naderian M, et al. The role of air pollution on ST-elevation myocardial infarction: a narrative mini review. Future Cardiol. 2018;14(4):301–6.
[33] Davoodabadi Z, Soleimani A, Pourmoghaddas A, Hosseini S, Jafari-Koshki T, Rahimi M, et al. Correlation between air pollution and hospitalization due to myocardial infarction. ARYA Atheroscler. 2019;15(4):161–7.