ASSESSMENT OF THE EFFECTS OF AIR POLLUTANTS ON BLOOD GLUCOSE CONTROL IN PATIENTS WITH TYPE 2 DIABETES

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ABSTRACT

Smart care is one of the elements of smart city, which has attracted the attention of many scholars to identify threats to the community's health. Air pollution has a significant contribution to diseases development such as type 2 diabetes, which is a major component of the global disease burden. The objective of this study is to investigate the effect of exposure to air pollutants such as NO_2, $PM_{2.5}$, and PM_{10} during 2016 on blood glucose control in Type 2 diabetic patients living in Tehran, capital of Iran. In this study, 124 diabetic patients of type 2 and partial correlation, odds ratio, and one-way Analysis of Variance have been considered to determine the effect of pollutants on the control of blood glucose in the patients. The results of this study verified that a significant positive correlation exists between NO_2 and blood glucose in women ($r = 0.43$; p-value < 0.001). There was also a relatively low but significant correlation in the female group between $PM_{2.5}$ and blood glucose have been identified ($r = 0.27$; p-value $= 0.033$). No significant correlation was found between pollutant PM_{10} and blood glucose in the patients. It is noteworthy that no correlation was found in the men's group for any of the pollutants.

1. INTRODUCTION

Diabetes mellitus doubles the risk of cardiovascular diseases and is the seventh leading cause of global mortality in 2016 (Coogan et al. 2016). Type 2 diabetes, known as adult diabetes, is caused by ineffective insulin use by the body. While obesity, sedentary and inactivity and other individual characteristics make diabetic risk factors, the potential role of air pollution has recently been mentioned as an etiological factor affecting these patients' health (Coogan et al. 2016).

Today, in many cities around the world, air pollution has become a peripheral dilemma and its survey is considered as a critical issue in urban management (Delavar et al. 2019). Therefore, given the high air pollution in developing countries, further research is needed on patients with type 2 diabetes (Eze et al. 2015).

In previous studies, the effect of air pollution on the incidence, occurrence, and mortality of type 2 diabetes was studied, and a limited number of studies were undertaken on the effect of air pollution on blood glucose control in type 2 diabetic patients. On the other hand, since blood glucose control is the primary way to prevent common diabetes complications such as heart disease, retinopathy, nephropathy, foot ulcer and amputation (Lucisano et al. 2017), it is crucial to identify the spatial factors affecting these patients' blood glucose control to reduce their complications and costs of treatment.

Environmental pollution is one of the most important risk factors in the spread of diseases (Eze et al. 2015). Inflammation and insulin resistance, which are signs of type 2 diabetes, are associated with exposure to nitrogen dioxide (NO_2) and fine particulate matter pollutants ($PM_{2.5}$ and PM_{10}) (Heidemann et al. 2014, O'Donovan et al. 2017). In an epidemiological study, the trend towards increased risk of insulin resistance, type 2 diabetes, and diabetes-related mortality is generally associated with increased air pollution (Heidemann et al. 2014). In a study in Iran, there was a positive correlation between children's exposure to PM_{10} and NO_2 and insulin resistance (Kelishadi et al. 2009).

The relationship between diabetes prevalence and air pollution has been examined in different studies. Eze et al. (2014) showed that increasing the concentration of the PM_{10} and NO_2 pollutants in the environment by 10 $\mu g/m^3$ is resulted in a 5.5 percent increase in the prevalence of diabetes, which was more clear for the PM_{10} pollutant. In the afore-mentioned study, pollutant concentrations in participants' residence were assessed by the average levels of pollutants over 10 years (Eze et al. 2014). Eze et al. (2015) showed that a 10 $\mu g/m^3$ increase in $PM_{2.5}$ and NO_2 pollutant concentrations raised the risk of type 2 diabetes by 8 to 10 percent (Eze et al. 2015). Also, Pearson et al. (2010) found a 0.92 percent increase in the prevalence of diabetes associated with a 10 µm rise in $PM_{2.5}$ concentration after adjustment for age, gender, annual income, education level, race, obesity, physical activity, latitude, and population density (Pearson et al. 2010). In another study by Honda et al. (2017), the chances of diabetes prevalence for people exposed to $PM_{2.5}$ and NO_2 pollutants were 35% and 27%, respectively (Honda et al. 2017).

Park et al. (2015) investigated the long-term effects of exposure to $PM_{2.5}$ and NO air pollutants on the prevalence and incidence

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of diabetes in people aged 45-84 years. In this study, the prevalence of diabetes was significantly associated with $PM_{2.5}$ (OR = 1.09, 95% CI: 1.00, 1.17) and NO (OR = 1.18, 95% CI: 1.01, 1.38) (Park et al. 2015).

In some studies, the effect of exposure to air pollution on the incidence of diabetes has been investigated. The results obtained by Balti et al. (2016) indicated a significant correlation between pollutants ($PM_{2.5}$ and NO_2) and diabetes incidence. The results showed a 13% and 11% increase in the rate of diabetes incidence with exposure to NO2 and $PM_{2.5}$, respectively (Balti et al. 2014). However, in another study by Park et al. (2015), none of the $PM_{2.5}$ and NO_2 pollutants were associated with diabetes incidence during a 9-year period (Park et al. 2015). The results of the study by Honda et al. (2017) showed that an increased interquartile range in $PM_{2.5}$ annual average led to a 1.4% rise in glycosylated haemoglobin (HbA1c) level, while this increase for NO_2 was equal to a 2% rise in HbA1c level.

In Iran, in 2006, the population of age groups ranging from 50 to 69 years old was equal to 10.36% and that of for more than 70 years old was 3.49%, which are estimated to be 27.4% and 7.8% in 2035, respectively (Aghamohamadi et al. 2018). Most of the reported studies regarding the impact of environmental pollutants on the epidemiology of type-2 diabetes have been conducted in developed countries (US, Canada, and Europe). With the high rate of type-2 diabetes prevalence in Iran and the country's increasing rate of aging population, as well as the problems of environmental pollutants especially in Tehran (which has a population of 8.3 million), further studies are needed in this regard. In addition, previous studies have examined the effect of air pollution on prevalence, incidence, and mortality of type-2 diabetes, while few studies have been conducted to monitor this disease and discovering the effective risk factors for controlling blood sugar in these patients. Therefore, investigating the impact of air pollution can play a significant role in controlling type-2 diabetes and, as a result, reducing its complications and therapeutic costs. Considering the necessity of this issue, we intend to conduct further studies on the effect of air pollutants on blood glucose control in type 2 diabetic patients. The aim of this study is to investigate the effect of exposure to air pollutants NO_2, $PM_{2.5}$, and PM_{10} on blood glucose in type 2 diabetic patients in Tehran.

In many studies, serum glucose has been used as a dependent variable to assess the impact of air pollution. Since serum glucose can vary widely over short periods of time, it is not a good idea to consider it as a dependent variable to evaluate the long duration of air pollution. On the other hand, glycosylated haemoglobin, which shows a long-term control of glucose and has a great predictive value for diabetes complications, has been examined in limited studies (ADA, 2018, Liu et al. 2016). Accordingly, in this study, HbA1c values have been used as outcome variables to investigate the effect of exposure to air pollution. Participants included 142 type-2 diabetic patients who were referred to the two Diabetes Clinic and Metabolic Diseases Centers of Endocrines & Metabolism Research Institute of Tehran University of Medical Sciences.

2. RESEARCH DESIGN AND METHODS

2.1 Participants and Clinical Assessments

In the present study, the information of 400 patients were collected from the two Diabetes Clinic and Metabolic Diseases Centers of Endocrines & Metabolism Research Institute of Tehran University of Medical Sciences, obtained from the patients' medical records in 2016. The input criteria for this study included type 2 diabetic patients and those who have registered their HbA1c values information in their medical records. Type-1 diabetic or pre-diabetic patients were excluded from our study. Thus, 142 type 2 diabetic patients remained in the study for analysis. Patients' characteristics and air pollution parameters are presented in Table 1.

2.2 Clinical measures

Participant clinical data were collected in 2016 including 3-month HbA1c values. Other clinical information includes body mass index (BMI), diabetes duration, information on lifestyle including physical activity and smoking status, demographic information including gender, age, marital status, educational status, and the exact address of patients' residence were also extracted from their medical records.

Characteristics		Gender			
		Female		Male	
		Mean	Count	Mean	Count
Age (year)		62		64	
BMI (kg/m^2)		30.33	82	26.60	60
Diabetes duration (year)		14	82	11	60
HbA1c_Spring (%)		7.39	82	7.41	60
HbA1c_Summer (%)		7.50	82	7.62	60
HbA1c_Fall (%)		7.56	82	7.48	60
HbA1c_Winter (%)		7.21	82	6.99	60
Marital	Married		69		58
	Single		5		0
	Divorced		7		0
Physical activity	No activity		23		16
	Walking		29		22
	Exercise		10		5
Smoking	Never		70		30
	Former		1		13
	Current		3		7
Education	<High school		34		7
	Diploma		32		25
	Some college		10		23
Employment	Householder		60		0
	Retired		11		31
	Employee		6		24
Medication	pills		52		35
	Insulin + pills		29		22
NO_2_Spring (μg/m^3)		51.35	82	52.77	60
NO_2_Summer (μg/m^3)		51.24	82	53.31	60
NO_2_Fall (μg/m^3)		54.03	82	55.90	60
NO_2_Winter (μg/m^3)		61.16	82	63.83	60
$PM_{2.5}$_Spring (μg/m^3)		19.35	82	21.18	60
$PM_{2.5}$_Summer (μg/m^3)		20.72	82	22.90	60
$PM_{2.5}$_Fall (μg/m^3)		26.63	82	28.68	60
$PM_{2.5}$_Winter (μg/m^3)		50.10	82	52.79	60
PM_{10}_Spring (μg/m^3)		74.22	82	72.97	60
PM_{10}_Summer (μg/m^3)		102.7	82	101.9	60
PM_{10}_Fall (μg/m^3)		96.22	82	95.22	60
PM_{10}_Winter (μg/m^3)		105.8	82	104.7	60

Abbreviations: Std.: Standard Deviation, BMI: body mass index, NO_2: Nitrogen dioxide, $PM_{2.5}$: particulate matter 2.5, PM_{10}: particulate matter 10 HbA1c: glycosylated haemoglobin

Table 1. Patients' and air pollution's characteristics

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2.3 Study Area

The area under study is Tehran District 6 with south western geographical location including Lon. = 51.38 and Lat. = 35.7 and northeast with Lon. = 51.42 and Lat. = 35.75 and 21.7 km^2 area is considered as the central regions of Tehran city. The addresses of all patients were geocoded on the map (Figure 1).

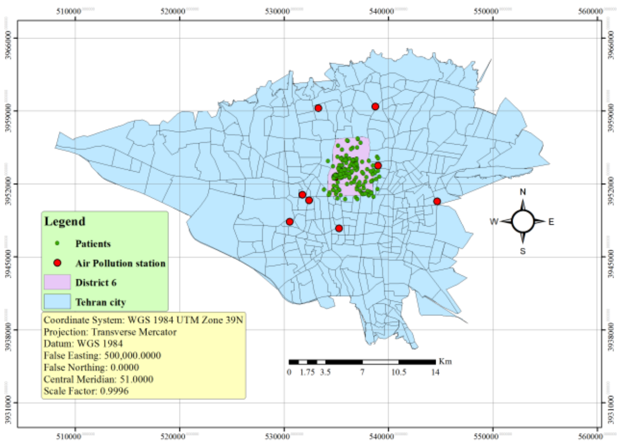

Figure 1. Case study and air pollution stations

2.4 Assessment of Exposure to Air Pollutants

Data on average daily levels of NO_2, $PM_{2.5}$, and PM_{10} air pollutants were collected from Tehran Municipality's Air Quality Control website (www.air.tehran.ir) for 9 stations around District 6 of Tehran (Figure 1) over one year from March 20, 2016, to March 20, 2017. Because of the existence of only one air pollution station in our study area, we used the model of air pollution prediction employed in Delavar et al. (2019) to estimate the pollutants in patients' residence. In this model, the elements of weather (wind speed and direction, minimum and maximum temperature, humidity), topography (X, Y, Z), weekdays and months of the year are used as predictor variables.

Since NO_2 air pollution is an essential gas pollutant in road traffic (Recio et al. 2016), we used the element of the area of streets in a 250-meter buffer to improve the estimation of pollutants. On the other hand, as the distance from the highway is used as an independent spatial pollutant predictor (Liang et al. 2018), we used the distance from the highway as another effective element in the estimation of pollutants. Then, the quarterly average of each pollutant was calculated in order to measure the exposure to air pollution for all participants' residences.

2.5 Statistical Analysis

Partial correlations have been employed to determine the correlations between air pollutants of NO_2, $PM_{2.5}$, and PM_{10} and HbA1c values of type 2 diabetic patients. Based on air pollutant quartiles and HbA1c quartiles, the Odds Ratio (OR) for the classified groups were calculated by considering the lowest quartile of the slight pollutant as the reference for exposure to the least air pollution. Furthermore, the one-way analysis of variance (ANOVA) was used to investigate the difference between HbA1c averages in quartiles of pollutants.

3. RESULTS

In Table 2, statistics of F = 3.29 indicates a significant difference of HbA1c between groups at a confidence level of 95%. Therefore, NO_2 pollutant increase was faced with a significant increase in the mean difference of HbA1c between groups in NO_2 quartiles in the female group (Figure 2). In Figure 2, the x and the y-axes represent NO_2 quartiles and the mean of HbA1c in each group.

	df	Mean Square	F	Sig.
Between Groups	3	5.58	3.29	0.026
Within Groups	64	1.69		
Total	67			
Abbreviations: df: degree of freedom, Sig.: significance				

Table 2. ANOVA test

Partial correlations between HbA1c and NO_2 pollutant after adjustment for control variables of age, duration of diabetes and BMI by gender segregation were significant just for women group with a correlation coefficient of 0.434 (p-value < 0.001) at 99% confidence level (Table 3). The results showed that women in the highest quartile of NO_2 air pollution in their residence had a tendency to higher levels of HbA1c compared to women in the lower quartile.

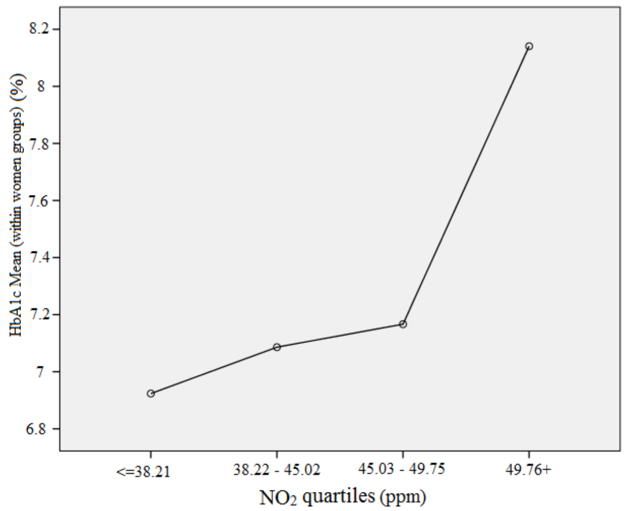

Figure 2. Mean plot into NO_2 quartiles

Gender		NO_2 Spring	NO_2 Summer	NO_2 Fall	NO_2 Winter
Female	Correlation	0.43*	0.40*	0.32*	0.24
	Sig. (2-tailed)	0.00	0.00	0.01	0.10
Male	Correlation	-0.06	0.01	-0.02	-0.28
	Sig. (2-tailed)	0.67	0.93	0.86	0.10
Control variables: Age, BMI and DD Dependent variable: HbA1c					
Abbreviations: DD: diabetes duration, BMI: body mass index, NO_2: nitrogen dioxide, HbA1c: glycosylated haemoglobin, Sig.: significance					

Table 3. Partial correlation results between HbA1c and NO_2 pollutant

NO2_Spring * HbA1c Cross-tabulation								
Gender: female				HbA1c (quartiles) (%)				Total
				≤ 6.30	6.31 - 6.95	6.96 - 8.15	≥ 8.16	
NO_2 (µg/m³)	Quartiles	≤ 38.21	Count	5	3	8	1	17
			% within NO_2	29.4%	17.6%	47.1%	5.9%	100.0%
		38.22 - 45.02	Count	9	4	3	4	20
			% within NO_2	45.0%	20.0%	15.0%	20.0%	100.0%
		45.03 - 49.75	Count	4	3	2	3	12
			% within NO_2	33.3%	25.0%	16.7%	25.0%	100.0%
		≥ 49.76	Count	1	5	4	9	19
			% within NO_2	5.3%	26.3%	21.1%	47.4%	100.0%
Total			Count	19	15	17	17	68
			% within NO_2	27.9%	22.1%	25.0%	25.0%	100.0%

Table 4. Cross tabulation for NO_2 and HbA1c

NO_2 (Spring)				
	<= 38.21 N=17 (reference)	38.22 - 45.02 N=20	45.03 - 49.75 N=12	49.76+ N=19
OR	1	2.2 (95% CI: 0.19 – 25.7)	3.75 (95% CI: 0.27 – 51.4)	45 (95% CI: 2.3 – 885.6)
Abbreviations: NO_2: nitrogen dioxide, OR: odds ratio				

Table 5. Odds ratio results for women in exposure to NO_2 air pollution

NO2 (Summer)			
	<= 37.85 N=22 (reference)	37.86 – 50.30 N=22	50.31+ N=21
OR	1	2.18(95% CI: 0.47 – 10)	5 (95% CI: 1.03 – 24.28)
Abbreviations: NO_2: nitrogen dioxide, OR: odds ratio			

Table 6. Odds ratio results for women in exposure to NO_2 air pollution

The odds ratio (OR) for NO_2 pollutant was calculated through cross-tabulation (Table 4). As shown in Tables 5 and 6, the odds ratio for NO_2 pollutant represents a 45% and 5% increase in patients' HbA1c levels with a 12- µg/m³ rise in average nitrogen dioxide concentration at their residence in spring (OR: 45; 95% CI: 2.28 – 885.6) and summer (OR: 5; 95% CI: 1.03 - 24.28), respectively.

According to Table 7, partial correlations between HbA1c and $PM_{2.5}$ pollutants after adjustment for control variables of age, duration of diabetes, and BMI in gender segregation only for women were significant with a correlation coefficient of 0.27 (p-value = 0.033), but the odds ratio for this pollutant was not significant at 95% confidence level. Also, the results of the survey of the correlation between HbA1c and PM_{10} pollutant were not significant for none of women and men groups.

Gender		$PM_{2.5}$ Spring	$PM_{2.5}$ Summer	$PM_{2.5}$ Fall	$PM_{2.5}$ Winter
Female	Correlation	0.27*	0.09	-0.11	0.17
	Sig. (2-tailed)	0.03	0.49	0.37	0.23
Male	Correlation	-0.16	-0.059	-0.13	0.03
	Sig. (2-tailed)	0.23	0.66	0.38	0.85
Control variables: Age, BMI and diabetes duration Dependent variable: HbA1c					
Abbreviations: BMI: body mass index, Sig.: significance					

Table 7. Partial correlation results between HbA1c and $PM_{2.5}$ pollutant

4. CONCLUSIONS

Given the development of advanced data collection technologies (e.g., biosensors and GPS), effective parameters (specifically, spatially factors) need to be identified in order to improve the decision-making process by knowing these parameters and determining the type and severity of their impact to take appropriate decisions on blood glucose control. To achieve this goal, we looked at the impact of air pollution and its severity on diabetic blood glucose control.

The results of this study confirm the correlation between exposure to NO_2 and $PM_{2.5}$ and blood glucose in type 2 diabetic patients. The results obtained by Honda et al. (2017) also showed a rise of 1.4% and 2% in HbA1c levels with exposure to an increased interquartile range in annual average values of $PM_{2.5}$ and NO_2, respectively (Honda et al. 2017). Also, a study by Chuang et al. in 2010 showed that exposure to air pollution (PM ≤ 10 µm) leads to a change in HbA1c (Chuang et al. 2010).

Additionally, according to our results in this research, exposure to NO_2 and $PM_{2.5}$ air pollutants for type 2 diabetic women affects their glucose control and can come to attention in the development of spatial decision support systems (SDSS). Similar findings in two studies on $PM_{2.5}$ and NO_2 also reported a stronger correlation between air pollution and type-2 diabetes in women compared to men (Pedersen et al. 2017, Eze et al. 2015).

The strength of this research is to use the accurate model for prediction of air pollution (RMSE = 1.79 μg/m^3) and to use elements of distance to highways and the area of streets around the patient's residence to improve the estimation of pollutants. The weakness of this research is its low sample size to achieve more statistically sound results.

Finally, according to our results, we suggested that air pollution could be considered as one of the effective potential predictor variables, especially for women, to decide to conduct a blood glucose control system for type 2 diabetic patients.

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