Preconception air pollution exposure and glucose tolerance in healthy pregnant women in a middle income country

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Abstract

Background: The effect of preconception exposure to air pollution on glucose tolerance during pregnancy in developing and middle-income countries is under debate yet. Therefore, this study aimed to assess the relationship between exposure to ambient particulate matter (PM) and traffic indicators with glucose tolerance in healthy pregnant women in Sabzevar, Iran (2019).

Methods: Accordingly, 250 healthy pregnant women with singleton pregnancies of 24-26 weeks of gestations were participated in our study. Land use regression (LUR) models were applied to estimate the annual mean of PM_1, $PM_{2.5}$ and PM_{10} at residential address. Traffic indicators, including distance from home to the nearest major road (DHMR) as well as total streets length in 100, 300 and 500m buffers around the home (TSL-100, 300 and 500) were calculated using the street map of Sabzevar. Oral glucose tolerance test (OGTT) was used to assess glucose tolerance during pregnancy. Multiple linear regression adjusted for relevant covariates was used to estimate the association of fasting blood glucose (FBG), 1-h and 2-h post-load glucose with PMs and traffic indicators.

Results: Exposure to PM_1, $PM_{2.5}$ and PM_{10} was significantly associated with higher FBG concentration. Higher TSL-100 was associated with higher FBG and 1-h glucose concentrations. Each one interquartile range (IQR) increase in DHMR the levels of FBG and 1-h post-load glucose were decreased -3.42 mg/dL (95% confidence interval (CI): -4.47, -2.37, P-value < 0.01) and -4.65 mg/dL (95% CI: -8.03, -1.26, P-value < 0.01), respectively.

Conclusion: We found higher preconception exposure to air pollution and exposure to air pollution during pregnancy were negatively associated with glucose tolerance during pregnancy in a middle income country.

1. Introduction

Gestational diabetes mellitus (GDM) has been associated with pregnancy complications, including macrosomia, hypertension, preeclampsia and premature birth and stillbirth [1]. In recent decades, the GDM prevalence increased in women [2] and about half of them have no classic risk factors for their GDM development [3]. The available evidence suggested that environmental pollutants, e.g., air pollution could act as a risk factor in developing GDM and glucose tolerance in healthy women [4–14]. However, the results of these studies are inconsistent. Some of these studies reported a significant relationship between exposure to PMs with impaired glucose tolerance (IGT) [6, 15, 16] and increased risk of GDM [7, 17, 18]; however, other evidence reported opposing results [8, 11, 15]. These studies used different diagnostic criteria and had limitations in the timing of GDM development [17]. Moreover, only three studies investigated the association of preconception air pollution exposure and GDM development [8, 17, 18].

The emerging evidence indicated that the pre-pregnancy period might be crucial time-window and higher exposure to pollutions could lead to decrease in GDM development [19]. So for, a very limited studies have been investigated the relationship between exposure to traffic indicators and PMs with glucose tolerance in healthy pregnant women [15, 16], and the available studies on the association of preconception exposure to traffic indicators and PMs with glucose concentrations obtained through oral glucose tolerance test (OGTT) have been exclusively conducted in high-income countries with no study available for low-middle-income or middle-income countries where urbanization is even more rapid. Given the variation in the observed associations between air pollution exposure and OGTT in different settings [8, 17, 18], it is not clear to what extent the results from high-income countries can be generalized to low-middle-income or middle-income countries. Therefore, this study aimed to examine the relationship between preconception exposure to traffic indicators as well as PMs concentrations at mother residence and OGTT results, a marker of glucose intolerance in healthy pregnant women in a middle income country (Iran).

2. Material And Methods

2.1 Study area

This cross-sectional study was conducted in Sabzevar (coordinates: 36°12' N 57°35', elevation: 977.6 m) a middle city in Khorasan Razavi province, Iran. Sabzevar is a city with an arid climate and annual average rainfall lower than 180 mm, the annual average temperature of 16°C and relative humidity of 43%. Based on the last census in 2016, the population of Sabzevar is 240,000 [20]. Figure 1 represented the air pollution monitoring station, street map and major roads of Sabzevar.

2.2 Population setting

The Ethics Committee of Sabzevar University of Medical Sciences approved this study (IR.MEDSAB.REC.1397.012). The pregnant women how were recruited to only Sabzevar Health Center for GDM screening during Jun 2019 to September 2019 were invited to this study. The inclusion criteria were including the gestational age of 24 to 26 weeks at enrollment, lived in Sabzevar during and before the pregnancy (at least one year) and singleton pregnancy. The exclusion criteria were including mothers who had GDM, preeclampsia, hypertension, change their residence during pregnancy and work outside of the home. From more than 5000 pregnant women who referred to the only Sabzevar Health Center for GDM screening, 250 of them had eligible criteria and applied to join in this study. Prior to entering the study, the inclusion/exclusion criteria, research aims and procedures were described to all pregnant women and all participants signed the consent form before enrollment. Socioeconomic information and lifestyle factors were obtained using a prepared questionnaire by face-to-face interviews.

2.5. Exposure assessment

2.5.1. Ambient particulate matter

The developed land use regression (LUR) models for Sabzevar were applied to estimate the preconception exposure to ambient PMs (i.e., PM_1, $PM_{2.5}$, and PM_{10}) and exposure to PMs during entire pregnancy at residential address. The details of developed models have been described in detail elsewhere [21]. Briefly, the PM_1, $PM_{2.5}$, and PM_{10} concentrations were measured using 26 air pollution monitoring stations installed in different parts of the study area. The LUR models were generated based on annual average of PMs concentrations. The main important variables which applied in developing LUR models were including urban morphology, population density, ten different land use, traffic and geographic location of monitoring stations. These generated models were able to predict 68%. 72% and 75% of the variation of annual PM_1, $PM_{2.5}$ and PM_{10} concentrations in Sabzevar. More details of LUR models validation are presented in Table S1 of Supplemental Materials.

2.5.2. Traffic density indicators

The traffic indicators, including total streets length in 100, 300 and 500 m buffer around the mother residence (TSL-100, 300 and 500 m) and distance from home to the nearest major road (DHMR) were calculated using Sabzevar street map, provided by Sabzevar municipality in ArcGIS v 10.5 software.

2.3 Glycemic status screening

During the study period, GDM screening in Iran was based on OGTT results. Glycemic status was assessed using 2-h, 75-g OGTT [22]. The OGTT was performed in the morning (8:00–9:00 AM) in the outpatient clinic, and the participants fasted for at least ten h prior to the tests. Normal glucose tolerance was determined according to the American Diabetes Association (ADA) criteria in 2008 [23]. Subjects with FBG $\geq$ 95 mg/dL at baseline, $\geq$ 180 mg/dL at 1-h, $\geq$ 155 mg/dL at 2-h were considered as normal glucose tolerance (NGT). The OGTT considered abnormal if one or two glucose concentrations exceeded mentioned concentrations. We excluded mothers who had one higher glucose concentration than NGT due to the different outcome of glucose homeostasis in pregnancy [24].

2.4. Glucose concentration measurement

The glucose oxidase method (Pars Azmoon, Tehran, Iran) and autoanalyzer (BT-3000) were applied to measure the venous serum glucose concentration of mothers in the reference lab of Sabzevar Health Center according to a standard clinical protocol.

2. 7 Statistical analysis

2. 7. 1 Main analysis

We developed linear regression models (MLR) to estimate the change in the FBG, 1-h and 2-h glucose concentrations associated with a one-interquartile range (IQR) increase in traffic indicators and PMs exposure (one at a time). The MLR models were further adjusted for a *prior* variable including maternal pre-pregnancy BMI (kg/m^2, continuous) and age (year, continuous), gestational age (week, continuous), parity (continuous), tobacco smoke exposure at home (yes/ no), abortion history (yes/no), family history of diabetes (yes/no) and two indicators of neighborhood socioeconomic status including percentages of unemployment and illiterate adults per census tract (based on the 2016 census). All statistical analysis was performed using Stata version 15 (Stata Corp LP, College Station, Texas). A significant level of 0.05 was applied for all analyses.

3. Results

3.1 Population setting

The statistical summary of the study participants and their PMs exposure as well as traffic indicators and FBG, 1-h and 2-h glucose concentrations are presented in Table 1. The median (IQR) age of pregnant women was 28 (8) years. The median (IQR) of pre-pregnancy BMI was 21.2 (5.9) kg/m^2. The median (IQR) of FBG, 2-hour glucose, and 2-hour glucose were 69 (8), 112 (35), and 100 (26), mg/dL, respectively. The median (IQR) of DHMR, TSL- 100, 300 and 500 m were 321 (388), 905 (257), 7756 (2035) and 20704 (6292) meters, respectively. Moreover, median (IQR) of estimated PM_1, $PM_{2.5}$ and PM_{10} were 40.8 (14.7), 47.4 (21.5) and 52.9 (23.7) μg/m^3, respectively (Table 1).

Table 1
Descriptive statistics of pregnant women, PMs and traffic indicators.

Variables	In study year
Pregnant Women characteristics	
Age (year); median (IQR)	28 (8)
Pre-pregnancy BMI (kg/m^2); median (IQR)	21.2 (5.9)
Gestational age (week); median (IQR)	26 (4)
Self-reported tobacco exposure at home	
Yes; N (%)	75 (30)
No; N (%)	175 (70)
Abortion history	
Yes; N (%)	90 (25)
No; N (%)	160 (75)
Family history of diabetes	
Yes; N (%)	24 (11)
No; N (%)	189 (89)
Parity (N); median (IQR)	2 (2)
Illiterate adults per census tract (%); median (IQR)	22.2 (15.3)
Unemployed adults per census tract(%); median (IQR)	7.0 (4.5)
Glucose concentrations (mg/dL); median (IQR)	
FBG	69 (8)
1-h post-load glucose	112 (35)
2-h post-load glucose	100 (26)
Particulate matter pollutants ($\mu g/m^3$); median (IQR)	
PM_1	40.8 (14.7)
$PM_{2.5}$	47.4 (21.5)
PM_{10}	52.9 (23.7)
Traffic indicators (m); median (IQR)	

Note: IQR: interquartile range; BMI: body mass index; FGB: fasting blood glucose

Variables	In study year
Total street length in a 100 m buffer	905 (257)
Total street length in a 300 m buffer	7756 (2035)
Total street length in a 500 m buffer	20704 (6292)
Distance to major roads	321 (388)
Note: IQR: interquartile range; BMI: body mass index; FGB: fasting blood glucose	

Spearman correlation of PM_1, $PM_{2.5,}$ PM_{10}, DHMR and TSL in different buffers at the residential address of pregnant women are shown in Fig. 1. There was a negative correlation between DHMR and PM_1, $PM_{2.5}$ and PM_{10} (r=-0.27, -0.25 and − 0.24, respectively). Furthermore, we observed a strong correlation between estimated PMs at residential address. A moderate positive correlation was observed between estimated PMs and total street length in 100 m buffer (r ranged from 0.18 to 0.32).

3.2. Main analysis

The results of the associations of exposure to traffic indicators and PM_s with FBG, 1-h and 2-h post-load glucose concentrations in healthy pregnant women are presented in Table 2. Overall, higher exposure to ambient PM_1, $PM_{2.5}$ and PM_{10} were associated with higher FBG. Moreover, higher TSL-100 m was associated with higher FBG and 1-hr. post-load glucose concentrations. Higher DHMR was negatively associated with FBG and 1-hr. post-load glucose concentrations (Table 2).

Table 2
Regression coefficient of exposure to air pollution with FBG, 1-h and 2-h post load glucose concentrations in health pregnant women.

Exposure	Outcome		β-coefficient (95% CI)	P_value
PM pollutants				
PM_1	FBG	Crude	0.80 (0.48, 1.11)	< 0.01
		Adjusted[a]	0.69 (0.37, 1.01)	< 0.01
	1-h post-load glucose	Crude	0.54 (-0.44, 1.53)	0.27
		Adjusted	0.30 (-0.68, 1.30)	0.54
	2-h post-load glucose	Crude	0.55 (-0.29, 1.39)	0.19
		Adjusted	2.37 (-2.75, 7.50)	0.36
$PM_{2.5}$	FBG	Crude	0.71 (0.38, 1.00)	< 0.01
		Adjusted	0.61 (0.28, 0.94)	< 0.01
	1-h post-load glucose	Crude	0.42 (-0.58, 1.4)	0.40
		Adjusted	0.22 (-0.79, 1.24)	0.66
	2-h post-load glucose	Crude	0.41 (-0.45, 1.28)	0.34
		Adjusted	2.65 (-2.59, 7.89)	0.31
PM_{10}	FBG	Crude	0.22 (0.04, 0.40)	< 0.01
		Adjusted	0.18 (0.00, 0.36)	0.043
	1-h post-load glucose	Crude	0.11 (-0.43, 0.66)	0.68
		Adjusted	0.07 (-0.46, 0.61)	0.78
	2-h post-load glucose	Crude	0.14 (-0.32, 0.60)	0.55
		Adjusted	2.22 (-0.54, 5.01)	0.11
Traffic indicators				
Street length in a 100 m buffer	FBG	Crude	2.70 (2.13, 3.27)	< 0.01
		Adjusted	2.64 (2.05, 3.22)	< 0.01
	1-h post-load glucose	Crude	3.46 (1.51, 5.41)	< 0.01

[a] Adjusted for the maternal age, pre-pregnancy body mass index, parity, gestational age, exposure to environmental tobacco smoke, percentage of illiterate as well as unemployed adults per census tract, abortion history and family history of diabetes

Exposure	Outcome		β-coefficient (95% CI)	P_value
		Adjusted	3.64 (1.65, 5.64)	< 0.01
	2-h post-load glucose	Crude	2.18 (0.49, 3.87)	0.01
		Adjusted	-2.50 (-13.14, 81)	0.64
Street length in a 300 m buffer	FBG	Crude	0.22 (-1.17, 1.63)	0.75
		Adjusted	0.24 (-1.17, 1.65)	0.73
	1-h post-load glucose	Crude	0.00 (-4.15, 4.16)	0.99
		Adjusted	0.49 (-3.7, 4.70)	0.81
	2-h post-load glucose	Crude	-0.36 (-3.92, 3.20)	0.84
		Adjusted	-4.11 (-25.90, 17.67)	0.70
Street length in a 500 m buffer	FBG	Crude	0.07 (-1.37, 1.52)	0.92
		Adjusted	0.07 (-1.39, 1.53)	0.92
	1-h post-load glucose	Crude	0.20 (-4.08, 4.50)	0.92
		Adjusted	0.67 (-3.88, 5.0)	0.76
	2-h post-load glucose	Crude	-0.55 (-4.22, 3.12)	0.76
		Adjusted	-8.66 (-31.17, 13.86)	0.44
Distance to major roads	FBG	Crude	-3.49 (-4.56, -2.43)	< 0.01
		Adjusted	-3.42 (-4.47, -2.37)	< 0.01
	1-h post-load glucose	Crude	-4.17 (-7.58, -0.75)	< 0.01
		Adjusted	-4.65 (-8.03, -1.26)	< 0.01
	2-h post-load glucose	Crude	-3.74 (-6.66, -0.82)	0.01
		Adjusted	-4.43 (-22.23, 13.37)	0.62

[a] Adjusted for the maternal age, pre-pregnancy body mass index, parity, gestational age, exposure to environmental tobacco smoke, percentage of illiterate as well as unemployed adults per census tract, abortion history and family history of diabetes

3.2.1. Associations with FBG

In fully adjusted models, a one-IQR increase in concentration of PM_1, $PM_{2.5}$ and PM_{10} was associated with increase of 0.69 mg/dL (95% confidence interval (CI): 0.37, 1.01, P-value < 0.01), 0.61 mg/dL (95% CI: 0.28, 0.94, P-value < 0.01) and 0.18 mg/dL (95% CI: 0.00, 0.36, P-value < 0.04) in FGB concentration.

Furthermore, one-IQR increase TSL-100 m was associated with an increase of 2.64 mg/dL (95% CI: 2.05, 3.22, P-value < 0.01) in FBG concentration. There was also a significant negative association between DHMR and FBG concentration (β = -3.42, 95% CI: -4.47, -2.37, P-value < 0.01). We did not find any significant association for TSL- 300 and 500 m and FBG.

3.2.2. Associations with 1-h post-load glucose concentration

Higher TSL-100 m was associated with higher 1-h post-load glucose concentration. In fully adjusted model, a one-IQR increase in TSL-100m was associated with an increase of 3.64 mg/dL (95% CI: 1.65, 5.64, P-value < 0.01) in 1-hr post-load glucose concentration. Moreover, a one-IQR increase in DHMR was associated with a decrease of -4.65 mg/dL (95% CI: -8.03, -1.26, P-value < 0.01) in 1-h post-load glucose concentrations. The associations of TSL-300 and 500 m, as well as PM_1, $PM_{2.5}$ and PM_{10}, were not statistically significant.

3.2.3. Associations with 2-h post-load glucose concentration

In this study, we did not observe any significant association between traffic indicators as well as PMs exposures and 2-h post-load glucose concentration (Table 2).

4. Discussion

To the best of our knowledge, this study is the first to evaluate the association of preconception exposure to traffic indicators and air pollution with the glucose concentration obtained in OGTT of healthy pregnant women in a middle income country. The main advantage of our study is the use OGTT results as a sensitive test for glucose homeostasis evaluations. We found that exposure to PM_1, $PM_{2.5}$ and PM_{10} was positively associated with FBG concentration, demonstrating that the levels of these pollutants might increase the risk of glucose intolerance. Moreover, TSL-100 m was positively associated with FBG and 1-h post-load glucose concentrations. Furthermore, DHMR was negatively associated with FBG and 1-h post-load glucose concentrations.

4.1. Available evidence

Given that this is the first study looking at the association between exposure to PM_1, PM_{10} and traffic indicators with FBG, 1-h and 2-h post-load glucose concentrations obtained in OGTT as indicators of glucose homeostasis in healthy pregnant women; we could not compare or finding regarding these pollutants with results of previous studies. However, a study by Lu *et al.* 2017 on the 3859 subjects aged over 30 years found that higher FBG, 1-h, 2-h and 3-h glucose concentrations in pregnant women who lived in areas with higher $PM_{2.5}$ level [16]. A part of this study (i.e., significant positive association between $PM_{2.5}$ exposures and FBG concentration) is in line with our findings; while, the associations of 1-h and 2-h glucose were inconsistent with our findings. Another study by Fleisch *et al.* 2014 on 2093 women found that second-trimester $PM_{2.5}$ exposure was associated with IGT occurrence but not GDM [15]. Choe et al. 2019 reported that $PM_{2.5}$ exposure in 2nd trimester was associated with GDM development [25]. A population-based retrospective cohort study by Shen *et al*. 2017, found higher $PM_{2.5}$ exposure during 12 week preconception period as well as first two trimesters of pregnancy was significantly associated with increase in the risk of GDM in pregnant women [18]. Moreover, the relationship between air pollution exposures and glucose homeostasis in non-pregnant healthy adults has been reported in previous studies. Peng *et al.* 2016 found that $PM_{2.5}$ exposure was significantly associated with increase in FBG concentration in non-diabetic subjects [26]. A study by Riant *et al*. 2018 on 2895 participants aged 40–65 years in France reported that PM_{10}exposure was associated with higher FBG and HbA1c [27]. A study by Chen *et al.* 2016, reported that short term exposure the PM_{10} (four days) was associated with higher FBG concentration as well as IFG occurrence [28]. A systematic review and meta-analysis by Elshahidi *et al*. 2019 found that higher $PM_{2.5}$ and PM_{10} exposures were associated with GDM development [29]. These reports are in line with our findings.

We found, FBG and 1-h post-load glucose concentrations were positively associated with TSL-100 m and negatively associated with DHMR. There is limited evidence that investigated the relationship between traffic-related air and noise pollution with glucose tolerance during pregnancy [24, 30, 31]. Hooven *et al.* 2009 investigated the association between residential proximity to traffic and outcome of glucose homeostasis during pregnancy and reported there was no significant association between traffic indicators and GDM occurrence [30]. Pedersen *et al.* 2017 examine the association of exposure to air and noise pollution in pregnant women and reported that there was no significant association of exposure to both pollutants and GDM development [24]. In contrast, Malmqvist *et al.* 2013 in a study based on birth registry data of 81,000 pregnant women in Sweden, found that exposure to traffic indicators was significantly associated with GDM development [31]. In our study, we found a positive correlation between TSL-100 m with PMs as well as a negative correlation between DHMR and PMs concentrations. Previous studies have shown that higher street length was significantly correlated with higher levels of PMs, especially in the smaller buffer sizes (e.g., 100 m) [20, 32–34]. These results could be explained our findings on the significant association of traffic indicators and glucose intolerance.

4.2. Biological plausibility

Although the precise mechanisms of the effect of traffic indicators and air pollution exposure on glucose tolerance are not fully understood, a number of potential mechanisms have been proposed. It has been shown that inhaled PMs into respiratory tract can pass through the alveolar cell and affect metabolism in extrapulmonary organs, e.g., liver [34, 35]. Similarly, non-water-soluble PMs with an aerodynamic diameter of ≤ 0.1 µm could alter glucose metabolism by entering the target cells [20, 36]. Another potential mechanism could be inhaled PMs that activate immunity cells, resulting in cytokines release [37, 38]. Some of these cytokines change glucose metabolism and hence glucose concentration in circulation [39]. Besides, inhaled PMs could induce an autonomic nervous system imbalance, which directly affected insulin sensitivity [40, 41]. Moreover, previous studies suggested that exposure to air pollution induces oxidative stress and adipose tissue inflammation, which disrupts insulin signaling and results in insulin resistance [42, 43]. Insulin resistance could in turn increase FBG, 1-hr, and 2-h glucose concentrations. Moreover, exposure to air pollution may also affect the methylation of genes related to glucose metabolism. The change in methylation patterns affects glucose concentration by altering peripheral insulin sensitivity during pregnancy [44, 45]. Finally, changes in glucose homeostasis in healthy pregnant women might be due to the metabolic induction change in the hypothalamus [46, 47]. Our results of the associations between traffic indicators as well as PMs exposures and glucose intolerance could be explained by one or all of the above mechanisms.

4.3. Strength and limitation

The advantage of our study included use novel markers, access to full residential address histories and detailed information on exposures. Moreover, we studied the preconception exposure to air pollution as well as traffic indicators and glucose homeostasis during pregnancy, which no considered in previous studies. Furthermore, this study is the first report of LMICs about air pollution exposure and glucose intolerance in pregnant women.

Our study has limitations as well. The sample size of our study was relatively small. We measured PMs exposure using the LUR models, and we did not measure individual exposure to PMs during and before pregnancy. Diet can also affect blood glucose concentrations during pregnancy, which was not assessed in our study. Furthermore, we did not evaluate the level of maternal stress that may affect blood glucose levels. These limitations should be considered in future studies.

5. Conclusion

We found higher PMs exposures were significantly associated with higher risk of glucose intolerance in healthy pregnant women. Moreover, we found a significant positive association between TSL-100 m and FBG and 1-h post-load glucose concentrations. Furthermore, a significant negative association was observed between DHMR and FBG and 1-h post-load glucose concentrations. Our finding provided evidence linking traffic indicators and PMs exposure with glucose homeostasis during pregnancy. If our results replicated by future studies could be a primary target in interventions to prevent glucose metabolism abnormalities. Moreover, our findings could offer evidence base for policymakers to implement interventions targeted at reducing adverse health effects of exposure to air pollution in urban pregnant women in our rapidly urbanizing world. However, further longitudinal studies with larger sample size are needed to confirm these results.

Declarations

Ethics approval and consent to participate

The Ethics Committee of Sabzevar University of Medical Sciences approved this study (IR.MEDSAB.REC.1397.012).

Consent for publication

Not applicable

Availability of data and material

The data are available from the corresponding author upon reasonable request.

Competing interests

All authors declare that they have no conflicting interests.

Funding

None

Authors' contributions

All of the authors contributed to the design of the study. M.Z., A.G and L.H collected the samples and air pollution data and wrote the first draft. H.H analyzed the data and wrote the first draft.. M.M. analyzed the data and design the statistical analyses and revised the manuscript. The paper and Supplementary Information were revised and approved by all the authors

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Figures

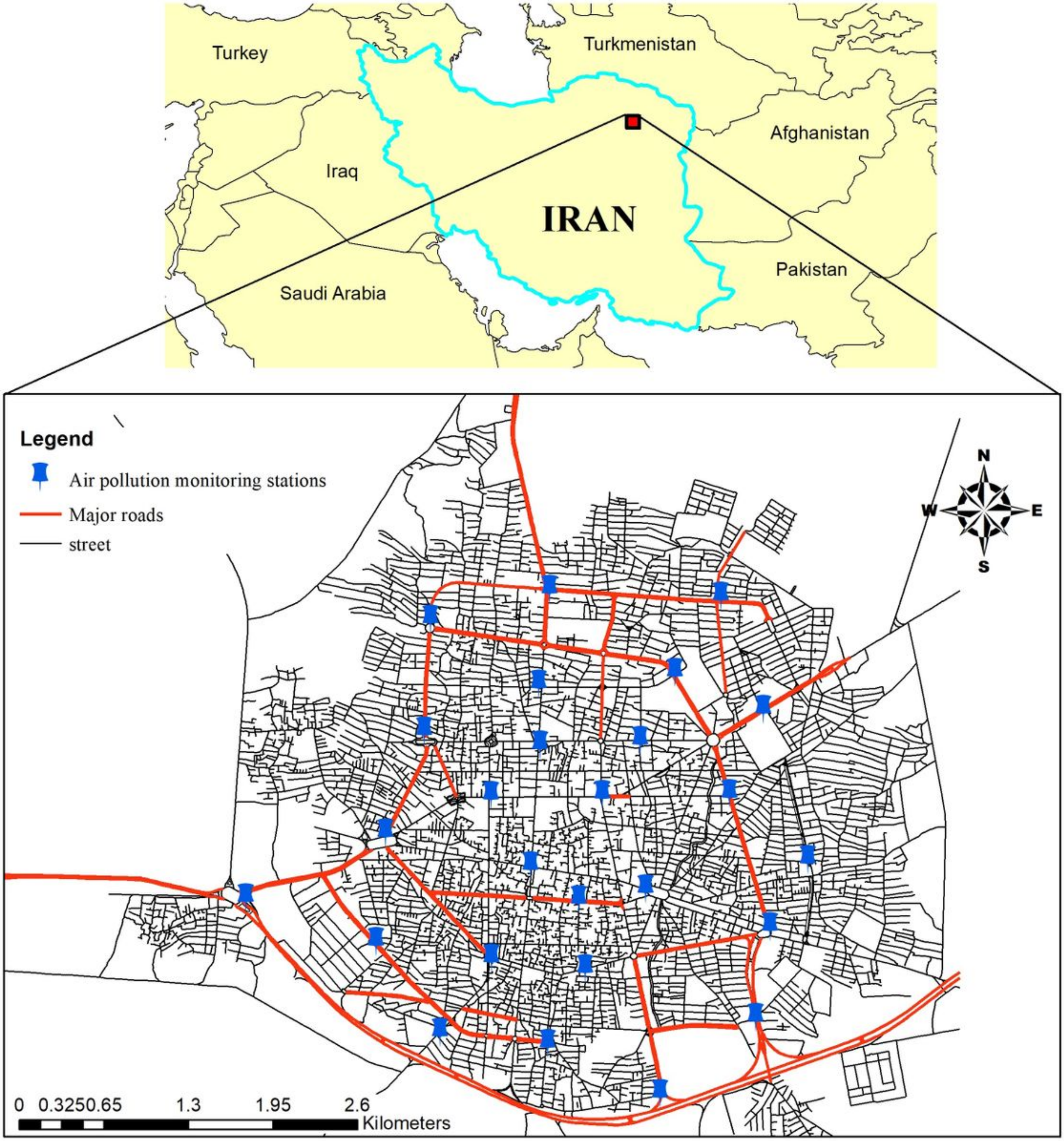

Figure 1

Study area, air pollution monitoring stations and major roads

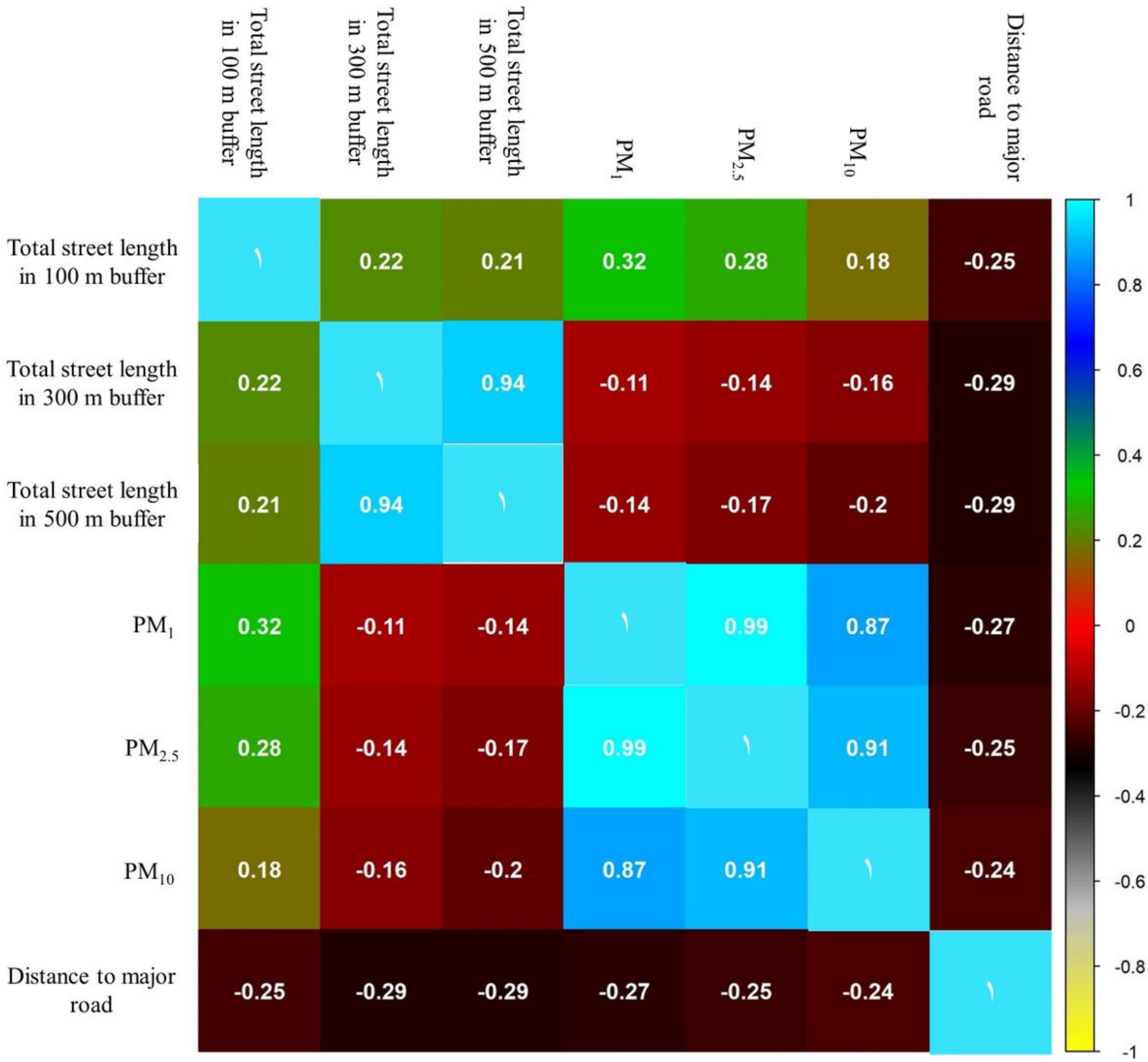

Figure 2

Spearman correlation between PMs and traffic indicators.

Supplementary Files

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